

## ETIOLOGICAL PROBLEMS IN UVEITIS

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Every ophthalmologist is able to settle the diagnosis of uveitis on the spot and he usually starts treating it immediately. But in most cases this treatment will be purely symptomatic.

We usually assume that uveitis is an inflammatory disease and at the same time we think of a reaction between some unknown antigen and a specific antibody. This reaction sets free histamine like products causing inflammation. Antiallergic drugs and steroids will certainly influence this reaction but will never reveal the etiology.

Many attempts have been undertaken to demonstrate specific antigen in the diseased eye, be it bacterial, viral or parasitic. Positive results for about every possible infective agent have been reported in the literature, but mainly on enucleated eyes. These findings are very important for our knowledge of endogenous eye diseases, but this kind of investigation did never have much clinical value. The percentage of positive results is much too low, most cases remain unsolved problems.

We have therefore paid more attention to the detection of specific antibodies in the eye. It must be said that despite the great work of A. C. Woods there is no reason to believe that a specific infection in the eye leads to an increase of specific antibodies in the blood or to an increased sensitivity of the skin. Very recent studies of Hallett, Wollowicz, Fera, Leopold and Wijewski and also of Coles have shown, that blood tests alone (Middlebrook Dubos Test for Tbc, Antistreptolysin O Test) are of no value in the diagnosis of uveitis cases. It is therefore very strange that everybody still believes very much in the diagnostical value of the Dye test (Sabín Feldmann) for the detection of toxoplasmosis. One should be aware that all these tests be it blood tests or skin tests can only be conclusive if they are negative. Then at least we know, that this kind of infection is very unlikely to be the cause of an eye infection.

We can assume that for practical purposes, a local antigen antibody reaction within the eye leads to a surplus of antibody. This antibody will most certainly remain fixed within the tissue. But part of it will leak into the blood stream, and part of it may get into the intraocular fluids (vitreous, aqueous humour). If we can determine these antibodies quantitatively within the blood, and at the same

time in the intraocular fluids, we may be able to find out, whether there is such a surplus or not. It must be said however that one is more likely to find such increased antibody concentration in the aqueous humour in cases of exudative anterior uveitis, than in cases of rather mild posterior choroiditis.

Antibodies are Gamma globulins. We can therefore establish a correlation between the total gamma globulin content and the final titer of a serological reaction. This ratio is called antibody activity. If we compare antibody activity of the serum and of the aqueous humour we get another ratio which we can call antibody activity ratio. Let us assume that all the antibody detectable in the aqueous humour of an inflamed eye were due to simple leakage of antibody through the damaged blood aqueous barrier, then this ratio should be equal to one. But if there really exists a surplus of antibody in the inflamed eye due to specific inflammation, then this ratio should be higher than one. Very recent experimental studies of uveitis in rabbits after intraocular injection of crystallized ovalbumin have again shown that this hypothesis can be proven. 10 to 15 days after the injection of the antigen a very marked infiltration with plasma cells and lymphocytes can be demonstrated in choroid and ciliary body. By means of a hemagglutination technique the antibody activity in the aqueous humour can be shown to be higher than in the serum. In a greater series of experimental leptospiral uveitis in rabbits the average antibody activity of the aqueous humour was three times as high as in the serum, while on the other side non specific aqueous humour (secondary aqueous humour in systemically immunized rabbits) had an activity three times lower than in the serum. Furthermore by using Coons technique with fluorescein labelled antibody it could be shown that the plasma cells in the iris and ciliary body contain specific antibody.

In clinical cases of uveitis the situation is much more difficult since the antigen is unknown. It is almost impossible to run more than three serological tests with the very small amount of aqueous humour available through puncture of the anterior chamber. One has therefore to decide which antibody one should look for. Our first studies were dealing with tuberculosis but we soon found out, that tuberculous uveitis is a very rare disease. We never found a percentage higher than 8 and in later years it went down to 5 and even to 1. It may be that this rare incidence of tuberculosis in the eye is due to the fact that this infection is very much decreasing in our population. But I am convinced that the diagnosis of Woods and others based on tuberculin skin test and the clinical picture were not true, many of these cases probably never were tuberculous.

Quite an amount of work has accumulated during the last ten years on ocular toxoplasmosis. There is no doubt that the Dye test of Sabin Feldmann is the most reliable reaction so far used. But one has to keep in mind that even for the Dye test the same thing is true as for all other serological tests: a positive reaction in the serum of a

patient with uveitis does not by any means prove the toxoplasmic etiology of this inflammation, even if it presents itself under the clinical picture of a posterior central choroiditis. There may be some reason to believe in a positive result only if—during the course of the disease—the titer of the reaction rises and later on drops down again when the local process is improving. A definite proof of toxoplasmic etiology can only be given by our method of quantitative serology in serum and aqueous humour. By means of this method we have found in a series of 217 cases a percentage of 7-10, which corresponds exactly with the results published by *Offret, Desmonts et coll* in France, using a very similar quantitative technique. It is very interesting to note that proven cases of ocular toxoplasmosis with high antibody activity of the aqueous humour did not have high serum titers, but rather low ones. This fact was also found by *Desmonts* and can perhaps be explained by an almost exclusively local (ocular) infection with toxoplasma. In this case it is likely, that only little antibody leaks out into the blood stream, a little more gets into the aqueous humour, but most of it will probably remain fixed at the site of inflammation. It must be mentioned however, that our method is not very sensitive and that we probably get negative results in cases, where only little inflammation occurs in the anterior part of the eye. We most probably miss the diagnosis in many cases, where only old scars are seen without signs of activity.

It seems that in Switzerland many people get infected with toxoplasmosis at an early age. A small survey on 150 blood donors 18 to 22 years old gave positive *Dye tests* in 57%. 20% had very high titers susceptible of fresh infection. None of these young men and women had any clinical signs of systemic infection.

As far as streptococcal infections are concerned, we come to the same conclusion as *Coles* and *Hallett and coll*: we do not think that the Antistreptolysine O test is of any practical value in the diagnosis of uveitis. We have not yet succeeded to work out a satisfactory micro method for the investigation of the aqueous humour. We therefore have run this test only in the serum, but our results were very disappointing.

It may be, that in so called rheumatoid uveitis, studies should be undertaken to demonstrate  $\beta_2$  A and M globulins in the aqueous humour and serum.

These are our results of the last 2 years. But I would like to say that there are numerous other infections possibly related with endogenous uveitis. One has to think of nematodes, leptospirosis, brucellosis, leprosy, rickettsiae, viral diseases and many others.

I have recently published a short paper on phacolytic uveitis, a very definite entity of intraocular disease the diagnosis of which can be established by a specific hemagglutination. It is very important that these cases—although clinically very similar—should not be taken as sympathetic ophthalmia. They can be cured by intra

capsular extraction of the lens, which is not always to recommend in true sympathetic ophthalmia

I hope that I have been able to show how difficult the etiological diagnosis of uveitis really is. It is therefore very unlikely that we ever will be able to know the cause of all our uveitis cases. Because of these difficulties we have to treat most patients on a presumptive diagnosis. But even if this treatment is often successful we should at least try to find out the cause of an endogenous uveitis. Our method of quantitative serology is only one way to accomplish this very tedious task.

### SUMMARY

The quantitative determination of specific antibodies in the inflamed eye is one way to find the cause of endogenous uveitis. In a positive case the antibody activity has to be definitely higher in the aqueous humour than in the serum. Clinical examinations with this method have shown that tuberculosis has become a rare disease; that significant toxoplasmosis titers were found in 7 to 10 per cent of the cases. The micro-methods for the antistreptolysine-O test in the aqueous humour are not yet satisfactory and have given disappointing results. Many other infections may be the cause of endogenous uveitis and the possibilities of quantitative serology are not yet exhausted.

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# IRIDOSCHISIS AND PROGRESSIVE ESSENTIAL IRIS ATROPHY

*A study of 20 patients with reference to the similarities in the clinical picture*

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When reviewing the results of treatment of glaucoma associated with progressive essential iris atrophy and iridoschisis a marked overlap in the clinical picture was noted in two cases\*. Since then more data have been collected and altogether five combined cases have been encountered. It is the purpose of this communication to present a short review of the entire series as well as to emphasize the diagnostic difficulties in the overlapping cases.

## MATERIAL

*Cases with progressive essential iris atrophy* (Table 1, cases 1 to 5)

Progressive essential iris atrophy is characterized by progressive atrophy and hole formation of the iris followed by displacement of the pupil. The entire structure of the iris, the stroma as well as the pigment epithelium, appears to be involved by the atrophy (Figures 1 to 3)

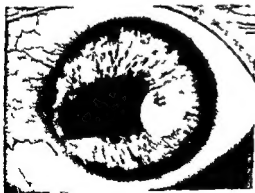


FIG 1 Case 2, right eye



FIG 2 Case 1 right eye

FIGS. 1 and 2 Cases of essential iris atrophy

(\*) Acta Ophth 39 356-366 1961



FIG 3 Case 19 left eye Essential iris atrophy A marked atrophy of the pigment epithelium as well as the stroma is noted



Fig 4a



Fig 4b

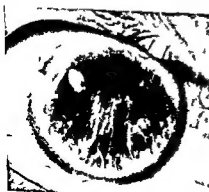


Fig 4c

FIG 4 Case 8 right eye with iridoschisis (a) before cataract extraction (b) following cataract extraction and (c) following discission of the iris membrane

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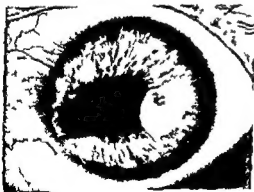


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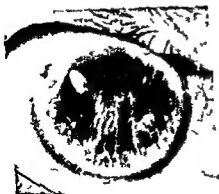


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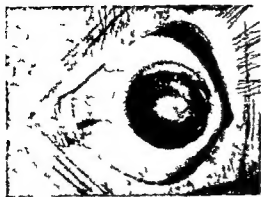


FIG 5 Case 9 left eye



FIG 6 Case 7, right eye

FIGS 5 and 6 Cases with iridoschisis



Fig 7a



Fig 7b

Fig 7b



FIG 7 Case 12 right eye with iridoschisis (a) and (b) before and after an iridectomy, (c) histopathology showing leiomyoma of the iris



FIG 8 Case 16 left eye

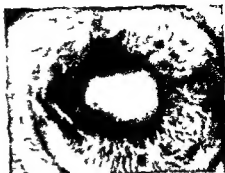


FIG 9 Case 17 left eye



FIG 10 Case 18 left eye

FIGS 8 to 10 Cases showing the characteristics of essential iris atrophy and iridoschisis

According to the literature however, the iris stroma is not detached from the pigment epithelium. The process appears to be idiopathic not related to previous inflammatory conditions of the eye. Glaucoma was present in six of the nine eyes with essential iris atrophy in our series.

#### Cases with iridoschisis (Table 1 cases 6 to 15)

In iridoschisis a detachment of the iris stroma from the pigment epithelium takes place. The stroma may be detached as a plane sheet or as separate strands (Figures 4 to 6). The changes are usually confined to the iris stroma the pigment epithelium not being involved by the process. The condition may occur as an idiopathic atrophy where no cause to the stromal detachment may be found. On the other hand there are cases with evidence of previous inflammatory or neoplastic condition. The cases 9, 10 and 11 presented evidence of chronic uveitis. To our surprise in one case (Table 1 case 12) iridoschisis was induced by leiomyoma of the iris (Figures 7a b c). The diagnosis was confirmed by the presence of myofibrils in the cytoplasm of the tumor cells. Two cases (6 and 8) were known diabetics.

TABLE I

ESSENTIAL IRIS ATROPHY							
	Sex	Age	Follow-up years	V 4	Tonometry	Chamber angle	Comment
Case 1 Marked bilateral essential iris atrophy	Female	21	3 years	R E 0 6 L E 0 35	P <sub>0</sub> = 6 mm Hg P <sub>0</sub> = 13	C = 27 narrow C = 0 27 narrow	Cyclodialysis 1929 Cyclodialysis peripheral iridectomy 1929
Case 2 Slight essential iris atrophy in the right eye	Female	25	8 years	R E 1 3 L E 1 3	P <sub>0</sub> = 13 P <sub>0</sub> = 13	C = 0 55 open (closed at the site of atrophy) C = 0 55 open	Iridectomy 1929
Case 3 Marked bilateral essential iris atrophy	Female	50	2 years	R E 0 1 L E 0 4	P <sub>0</sub> = 16 P <sub>0</sub> = 15	C = 0 32 closed C = 0 37 open	Iridectomy 1929 Retinoschisis Prophylactic Iridectomy 1929
Case 4 Bilateral essential iris atrophy	Male	77	1 year	R E 0 15 L E 0 25	P <sub>0</sub> = 20 P <sub>0</sub> = 22	C = 0 17 open C = 22 open	
Case 5 Bilateral essential iris atrophy	Female	55	1 month	R E 0 35 L E 0 25	P <sub>0</sub> = 8 P <sub>0</sub> = 17	C = 0 28 open with synechias C = 0 36 narrow	Acute glaucoma Iridectomy 52

TABLE I—Contd

IRIDOSCHISIS									
Case 6 Iridoschisis in the right eye	Female	61	2 years	R E 0 2 L E 0	P = 15 P = 80	C = 0 25 open C = 0 closed	Diabetic retinopathy cataract extraction 1939		
Case 7 Marked iridoschisis in the right eye senile iris atrophy in the left	Female	55	6 years	R E 0 08 L E 0 08	P <sub>+</sub> = 9 I <sub>+</sub> = 16	C = 0 28 not visible C = 0 % open	Iridocyclitis 1935 Iridectomy 1945		
Case 8 Marked iridoschisis in the right eye	Female	75	7 years	R E 0 01	P <sub>+</sub> = 14	C = 0 % open	Diabetic retinopathy Cataract extraction 1959 Discussion of the iris 1959 Big scleral staphyloma		
Case 9 Iridoschisis in the left eye	Female	55	2 years	R E 0 2 L E 1 00	P <sub>+</sub> = 12 I = 11	C = 0 32 not visible C = 0 33 not visible	Iridoid degeneration of the cornua		
Case 10 Iridoschisis in the right eye	Male	50	1 year	R E 0 5 L E enucleation for perforating injury 1959	P <sub>+</sub> = 19	C = 0 20 open	Chronic uveitis		



TABLE 1—Contd

IRIDOSCHISIS	Sex	Age	Follow-up years	I I	Tonography	Chamber angle	Comment
Case 11 Iridoschisis in the left eye	Female	25	1 year	R E 1 0 L E 0 0	P <sub>0</sub> = 14 P <sub>0</sub> = 0	C = 0 31 open C = 0 31 open	Iris blue Chronic uveitis from the age of 8 months Corneal diameter 9 mm Iris yellow brown
Case 12 Iridoschisis in the right eye	Male	22	1 year	R E 0 01	P <sub>0</sub> = 16	C = 0 26 open iris threads attached to Schwalbe's line in upper nasal quadrants	Iridectomy for congenital cataract PAD letomyoma
Case 13 Marked iridoschisis in the left eye	Female	44	1 year	L E 1 6 R E 1 3 L E 1 3	P <sub>0</sub> = 14 P <sub>0</sub> = 20 P <sub>0</sub> = 16	C = 0 31 open C = 0 30 open C = 0 26 closed	Perforating injury in the childhood
Case 14 Iridoschisis in the left eye	Male	70	1 year	R E 0 0 L E 0 0b	P <sub>0</sub> = 17	open with synchias	Phthisis Cataract extraction 20 years ago
Case 15 Iridoschisis in the right eye	Male	36	2 months	R E 1 0 L E 1 0		open with synchias open	

TABLE I *Contd.*

CASES WITH FEATURES BOTH OF ESSENTIAL IRIS ATROPHY AND IRIDOSCHISIS									
	Age in years	Sex	Duration in years	R E	L E	P	C	Remarks	Outcome
Case 16 R F. Essential iris atrophy L F. Essential iris atrophy and iridochisis	65	Male	2 years	R E 0.75 L E 0.6	P 6		C 0.25 narrow with synchias	Cyclodialysis 1951 Cyclodialysis 1943	
Case 17 R E. Iridochisis L F. Essential iris atrophy and iridochisis	69	Female	2½ years	R F 0.01 L E 0.2	P 7	1½	C — large open C — 0.21 open with synchias	Old thyroiditis Iridectomy 1960	
Case 18 R F. Iridochisis L F. Essential iris atrophy and iridochisis	73	Female	4 years	R F 0.08 L E 0	P — 9	P — 66	C — 0.21 narrow but open C 0 closed	Cataract extraction 1959	
Case 19 R L. Essential iris atrophy and iridochisis	71	Male	16	R L 0 L F 0.55	P 1 — 53	P 19	narrow with large synchias open		
Case 20 R L. Essential iris atrophy L L. Essential iris atrophy and iridochisis	37	Male	1½	R F 1.0 L E 1.0	P — 17 P — 17		C — 0.22 C — 0.27		
DYSGENESIS MESODERMALIS									
Case 21	Female	9	5	R F 0.2 L F 1.8	P 16 P — 33		C — 0.25 narrow with large synchias C 0.03 closed	Indentation 1961	



FIG 11a Case 21 right eye with dysgenesis mesodermalis. The pupil has disappeared under the limbus at 11 30 o'clock

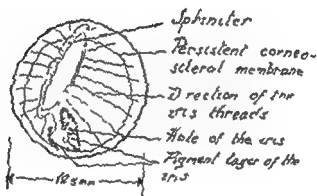


FIG 11b The same eye as in FIG 11a but for years earlier. The pupil is slit like

Cases with the characteristics of essential iris atrophy and iridoschisis (Table 1, cases 16 to 20)

The overlap in the clinical picture was noted in five of the ten eyes of cases 16 to 20 (Figures 8 to 10). The opposite eyes showed either essential iris atrophy (cases 16, 19, and 20) or iridoschisis (cases 17 and 18). The overlap was confusing and rendered difficulties in the diagnosis. The cause of the overlap is unknown. One reasonable assumption, however, that in essential iris atrophy the deeper layers of the stroma would show a more advanced atrophy resulting to the splitting. As a matter of fact this probably took place in one case (number 19). In 1960 marked iris atrophy was noted in the left eye without evidence of splitting. Two years later definite iridoschisis had developed. In iridoschisis on the other hand, the displacement of the pupil would require the pigment epithelium to be involved by the atrophy at the same time.

As a differential diagnostic point a case with dysgenesis mesoder malis corneae et iridis is presented (Table 1, case 21) (Figure 11) This condition is often seen in children and is of hereditary nature, whereas no hereditary patterns were observed in the cases 1 to 20

According to the literature essential iris atrophy is mostly seen in young females whereas patients with iridoschisis are usually old In the present series four of the five patients with essential iris atrophy were females but both conditions were seen in young and old individuals without any clear cut predilection to age

## ASPIRATION OF CONGENITAL CATARACT

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Aspiration of cataracts is an old technique, dating back to biblical times. Refinements of the crude techniques took place, until currently when aspiration is conducted manually and by motor suction. It is the latter method which is featured in this paper. Motor aspiration of congenital cataract has been carried on at the New York Eye and Ear Infirmary during the past three years. The technique is as follows:

### PREOPERATIVE STUDY

The pupils are dilated maximally. Those which do not achieve full dilatation require full bilateral iridectomy at time of surgery. Others do well on one or two peripheral iridectomies. Biomicroscopic study determines the size, nature and density of lenticular lesion, and any other anterior segment pathology, if present.

### SURGERY

General anesthesia is used for all cases. Narrow angle keratome section is made at the superior limbus. The keratome penetrates directly into the lens nucleus, liberating lens matter into the anterior chamber. The Kara aspiration needle, connected by tubing to a motor pump, is introduced through the same incision. The needle is a specially designed, thin walled needle, 18 gauge with a 17 bore, flattened at the distal end and dulled at the tip. The motor aspiration is controlled by a foot pedal. The suction is calibrated at 40 cm Hg. The aspiration is intermittent, under direct observation. For better visualization of the cataract remnants during the aspiration the ultra violet light may be used. The end point is a clear pupil, with a Ring of Soemmering behind the iris. When this is achieved the iridotomy or iridectomy is performed, the wound is closed with one or two 6-0 chromic sutures, and air is injected into the anterior chamber. Atropine, 1 per cent, is instilled. These eyes are kept dilated for one month following surgery.

With the zonular cataract, some modification of the technique is called for. After the keratome section, the cystotome is introduced into the anterior chamber and the lens matter is stirred prior to aspiration. The latter may be performed immediately, or forty-eight hours later, if it is preferred to wait for full maturation of the cataract.

The posterior capsule is usually peeled off the anterior vitreous face by this technic and coils away from the pupillary axis

#### DISCUSSION

The technic outlined above is essentially a linear extraction at one sitting. In our hands it has been less traumatizing than the usual methods of management of congenital cataracts. The surgery is of less than five minutes duration; minimum intraocular penetrations are necessary; the child is kept under general anaesthesia for a minimum period of time. I emphasize this latter statement because I have witnessed congenital cataract surgery on infants which lasted one to one and one half hours.

Thus far twenty five cases have been operated at the Infirmary according to the technic outlined above.

#### Complications

Secondary membrane 2 cases Required discussion Good subsequent postoperative result

HypHEMA 1 case Resorbed, with no deleterious effects

Updrawn Iris 1 case Required sphincterotomy

Ages ranged from 6 months to 12 year. Over half were under 5 years of age; the vast majority having bilateral cataracts. In four patients, the lens changes were hypermature, and bilateral surgery was performed a week apart.

#### Vision

Because of the youth of the patients it was difficult to obtain accurate visual recording soon after surgery. Gross approximations were made e.g. observation as the child picked up objects from the floor. It is interesting to note that a corrected vision of 20/20 is rare after congenital cataract surgery. The vast majority of patients achieve from 20/30 to 20/50 (even in uncomplicated cases!). This indicates that a cataract is merely one feature of an eye which may have multiple congenital aberrations e.g. poorly developed macula.

Results obtained thus far encourage us to continue this technic until a large enough series, with a sufficiently lengthy postoperative follow up, is achieved so as to evaluate properly motor aspiration of congenital cataracts as compared with other methods of surgical treatment of this condition.

## AN ESTIMATION OF THE REFRACTIVE INDEX OF THE HUMAN LENS IN VIVO

JIN OTSUKA, M.D. TAKASHI TOKORO, M.D., MINORU ARAKI, M.D.

(Department of Ophthalmology of Tokyo Medical and Dental University)

### INTRODUCTION

In physiological optics of the human eye, the crystalline lens is regarded to be a homogeneous refractive element and to have a constant value of the refractive index. Under these assumptions, many diverse values of the refractive index of the lens have been adopted by many authors for phacometry, as shown in Table I.

TABLE I

1.437	HELMHOLTZ
1.43	ZEEMAN, AMERBACH, TRON
1.416	SORSBY, YOSHIMOTO
1.41	TSCHERNING
1.409	TANI, OTSUKA, TOKORO

Then, a series of experiments on the phacometry of the human lens and the ultrasonography of the eye was done. It was found that the axial length of the eye determined by the ultrasonography did not coincide with the axial length calculated from phacometry using these previous values of the refractive index. Such a discrepancy must be due to the assumptions inherited in phacometry, among which the assumption of the refractive index of the lens is the most fundamental. Therefore, an attempt was made to search a new value of the most suitable index for physiological optics.

### METHOD

For this purpose we devised an apparatus for photographic phacometry and for ultrasonography (Fig. I, Fig. II).

For 46 normal human eyes from 9 to 21 years of age, 1% atropin was used topically in order to attain cycloplegia. For these eyes, the axial length, the depth of anterior chamber and the thickness of the lens were measured by means of the ultrasonography. The power of the lens was calculated using the refractive index of the lens of 1.409 for horizontal and sagittal meridians. The axial length of the eye was then

calculated. In performing the phacometry, Fuchsian Sanson's images for both horizontal and sagittal meridians were obtained and therefore two values for the axial length of the eye were calculated. Then, we averaged both values and regarded them to represent the axial length of the eye.



FIG 1



FIG 2

#### COMPUTATION <sup>4</sup>

The equation that is  $l_p = F \{r_1, d_1, d_2, P_1, P_2, P_3, A, n_2\}$ —(1) determines the relations of the refractive index of the lens and other optical constants.  $l_p$  calculated axial length for phacometry  $r_1$ , radius of the anterior surface of the cornea  $d_1$ , depth of the anterior



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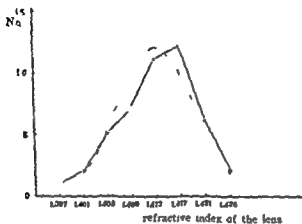
## METHOD

For this purpose, we devised an apparatus for photographic phacometry and for ultrasonography (Fig I, Fig II).

For 46 normal human eyes from 9 to 21 years of age, 1% atropin was used topically in order to attain cycloplegia. For these eyes, the axial length, the depth of anterior chamber and the thickness of the lens were measured by means of the ultrasonography. The power of the lens was calculated using the refractive index of the lens of 1.409 for horizontal and sagittal meridians. The axial length of the eye was then

On the other hand, the refractive power of the lens is fairly constant over whole range of refraction. Therefore, it seems to be evident the change of the axial length is the most important factor in the genesis of myopia.

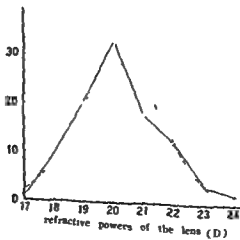
FIG III



average 1.413

standard deviation of  $\pm 0.006$

FIG IV



average 20.21

standard deviation of  $\pm 1.39$

chamber,  $d_2$ , thickness of the lens,  $P_1, P_2, P_4$ , distances of the Purkinje-Sanson's images,  $A$ , refraction,  $n$ , refractive index of the lens). When the refractive index of the lens is regarded to be a variable, the 11th power of function of  $n$  is obtained and it is very difficult to solve. So we took a simple way for it.

First, we assume  $n = 1.409$  and put this value into the equation (1) and  $l_p$  is calculated.

Next, we took a total differential of the equation (1),

$$dl = \pm \sqrt{\left(\frac{\delta l}{\delta r_1}\right)^2 (dr_1)^2 + \left(\frac{\delta l}{\delta d_1}\right)^2 (dd_1)^2 + \left(\frac{\delta l}{\delta d_2}\right)^2 (dd_2)^2 + \left(\frac{\delta l}{\delta P_1}\right)^2 (dP_1)^2 + \left(\frac{\delta l}{\delta P_2}\right)^2 (dP_2)^2 + \left(\frac{\delta l}{\delta P_4}\right)^2 (dP_4)^2 + \left(\frac{\delta l}{\delta A}\right)^2 (dA)^2 + \left(\frac{\delta l}{\delta n}\right)^2 (dn)^2}$$

where,  $r_1, d_1, d_2, P_1, P_2, P_4$  and  $l$  are small constant values and these errors are already estimated, that is,  $r_1 = 7.7$  mm,  $d_1 = 3.6$  mm,  $d_2 = 3.6$  mm,  $P_1 = 0.9$  mm,  $P_2 = 1.8$  mm,  $P_4 = 0.6$  mm,  $A = -3.0$  dptr,  $n = 1.409$ ,  $dr_1 = \pm 0.003$  mm,  $dd_1 = \pm 0.03$  mm,  $dd_2 = \pm 0.03$  mm,  $dP_1 = \pm 0.002$  mm,  $dP_2 = \pm 0.01$  mm,  $dP_4 = \pm 0.002$  mm,  $dA = \pm 0.25$  dptr. Then,

$dl = \pm \sqrt{0.014055 + (-77.488)(dn)}$  — (3) is obtained.  $l_u - l_p$  ( $l_u$ , measured axial length for ultrasonography), that is  $dl$ , is regarded to be the errors of the axial length. Therefore, the inferred index of  $1.409 \pm dn$  is obtained and put this value into the equation (1) again and the axial length is calculated repeatedly until  $dl$  reaches to an infinitely small value. Then,  $n_2$  is calculated.

## RESULT

The refractive index of the lens calculated for 16 normal human living eyes averaged 1.413 with standard deviation of 0.006, when the accommodation is relaxed by the use of topical atropine and the distribution curve of the index proved to be binominal as Fig. III.

Using this value of the refractive index, we determined the power of the lens for 154 human eyes. An average of 20.21 diopters with standard deviation of  $\pm 1.39$  diopters was obtained. The distribution curve is fitted to a binominal curve as shown in Fig. IV. Moreover the axial length was computed therefrom.

The whole sample was divided into classes according to their refraction and the power of the lens, the axial length and the power of the cornea were plotted for each class of refraction. Connecting the average values in this plot, the curves were obtained as shown in Fig. V. The higher the myopia is, the longer the axial length.

On the other hand, the effects of gamma angle in the phacometry were tested using model eyes which consisted of an optically grinded glass shell and a lens mounted with a metal ring and of an artificial anterior chamber filled with water in between them. The curvature of all surfaces and the refractive index of the material of the model eyes were known with accuracy. Rotation of 5 degrees of the model eyes resulted in errors of less than 0.5% in the radii of the anterior and the posterior curvature of the lens. This error makes a difference of the axial length of less than 0.003 mm which is considerably less than the accidental errors of the ultrasonography. Therefore the neglected gamma angle makes no appreciable errors in the present calculation of the refractive index.

Secondly, the refractive index obtained in the present study does not mean any true refractive index of the lens material, since the neglected posterior corneal surface alone can make the difference of 0.007 in the index. The refractive index of the lens calculated without the neglected posterior corneal surface is higher than the case with the neglected one. This consideration shows therefore that the neglected posterior surface is not the reason why we got higher refractive index than the Gullstrand's value. For calculations in physiological optics most authors neglect the posterior surface of the cornea since it is very difficult to measure the curvature of it with accuracy. So far as the physiological optics is concerned the present value seems to be valid and important.

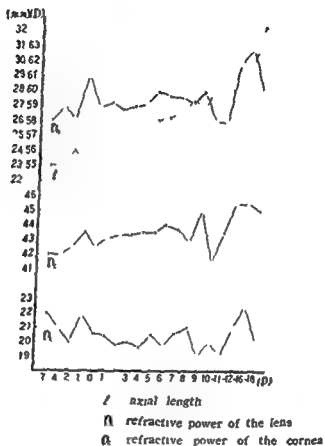
Thirdly, when we consider the accidental errors of phacometry and ultrasonography, the standard deviation was estimated to be 0.008. This calculation however was made assuming that the differences of the values for the axial lengths obtained by phacometry and ultrasonography were entirely due to the errors of the index. If the deviation of the value for the neglected elements for example, the curvature of the posterior surface of the cornea, non-spherical anterior and posterior surfaces of the lens, individual variations of the velocity of the ultrasonic waves in the media etc. were taken into account, the actual deviation of the refractive index may become smaller. Sorsby mentioned in his studies on emmetropia and its aberrations that the deviation of the total refractive index of the lens seems to be negligible in calculating constants of optical elements of the eye. The deviation of the index obtained by our experiment was less than 0.008 and this result may offer a very good evidence in support of Sorsby's statement.

Sorsby also mentioned that the axial length calculated from phacometry were shorter than those measured with X-ray vision. In the present work the calculated axial lengths in phacometry were longer than that measured with ultrasonography. The reason why we have got an opposite result to that of Sorsby is probably due to the fact he used the higher value for the refractive index of the lens, that is 1.416 than 1.409 which was used in our calculation. The present refractive index of the lens 1.413 may therefore be used as the most

## DISCUSSION

The assumptions set in phacometry are that the gamma angle and the posterior surface of the cornea were neglected and the crystalline lens was regarded to be homogeneous. These assumptions will now be discussed.

FIG. V



First, the phacometry was performed with regard to the optical axis of the eye, while the ultrasonography was done with regard to the visual axis. The difference between two axes, that is, gamma angle was neglected. Changes of the corneal curvature, when the eye is rotated around 5 degrees, that is, an average value of the gamma angle, were shown by Noto to be less than 0.01 mm which leads to a difference of only less than 0.06 mm of the axial length by calculation. According to Tornquist the difference of the values of these axes make only negligible difference in the measured depth of the anterior chamber. The centre of the rotation of the eye locates near the posterior pole of the lens and therefore the neglected gamma angle should not make any appreciable errors in the measurement of the lens thickness.

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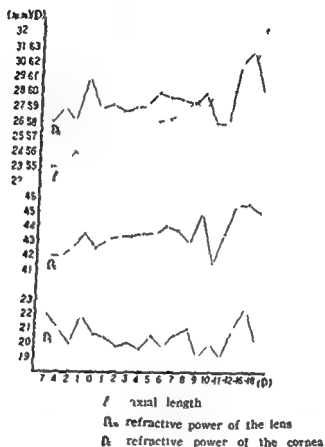
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## PRODUCTION OF CATARACTS BY THE INTRALENTICULAR INJECTION OF ENZYMES AND ENZYME INHIBITORS

SHOCH, D, VAIL, D and ZELLER, E A,  
(with the assistance of E A Andujar), USA

The lens epithelium appears to be the major target of most chemical and physical agents which have been used previously to produce experimental cataracts. Recently we developed a new procedure by injecting *in vivo* certain compounds directly into the lens and thus bypassing the epithelium (XVIII Consilium Ophthalmol, abstracts, p 713). Thus far two classes of substances, haloacetates and proteases, have turned out to be effective. To gain some insight into the action of these cataractogenic substances, the sequence of morphological changes which appeared after the intralenticular injections were followed. In addition, certain facets of the protein metabolism of the opaque lens were investigated, e.g. by determining the protein and non protein content and the aminopeptidase activity. Into one eye of rabbits  $2.5\mu$  moles of iodoacetate or  $25\mu$  g of crystalline papain were injected while the other eye received the solvent alone. Statistical analysis of the results obtained after 10, 20 and 30 days revealed that the administration of iodoacetate was more efficient than that of papain in reducing protein content and peptidase activity. In neither case was the loss of protein compensated by higher non protein values.

## ABNORMAL PROTEIN METABOLISM AS THE CAUSE OF DEVELOPMENT OF CATARACT IN OCULAR LENS\*

ANIMA DEVI, Ph D

Department of Biochemistry, Faculty of Medicine,  
Laval University, Quebec Canada

If the development of cataract in ocular lens is the result of an accumulation of denatured protein it is possible that it has been caused by a progressive loss of hydrolytic activity of inter and intra cellular proteases in the lens. The mechanism of protein synthesis may also be impaired so that these intracellular cathepsin like enzymes, so vitally important in removing the denatured proteins, are not synthesized to the extent as necessary. Whatever may be the cause of the development of cataract it can be said that it is in some way connected with a defect or defects in protein metabolism. In the present communication I would like to discuss this aspect of protein metabolism which appears to be responsible for cataract development.

The ocular lens as we know, contains the highest percentage of protein than any other tissue of the body and is mostly made up of an albumin like protein. To maintain the transparency, the lens must have a very active mechanism for the removal of denatured proteins as well as for the synthesis of proteins. In other words there should exist a dynamic equilibrium between the processes of protein anabolism and catabolism in lens if the transparency of the lens is to be preserved. Any abnormality in any one of these two processes should lead to the development of cataract.

The importance of intracellular proteolytic enzymes in the development of certain types of cataract was first recognized by Borden Cooper (1) Goldschmidt (2) and others (3) as far back as 1914 and 1925 although definite evidences first appeared from the work of Zeller and Devi (4). These investigators reported that they observed a gradual loss of proteolytic activity of a chymotrypsin like enzyme in the lens during the progressive development of cataract induced by x rays.

The autolysis of lens proteins was first noted by Clapp (5) and extensively investigated at a later date by Krause (6). Zeller and Devi (4) in their studies used manometric methods for the measurement of protease activity in lens homogenate. The method was based on the liberation of  $\text{CO}_2$  by the enzymatic hydrolysis of synthetic

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(\*) This work has been supported from a grant (no MA 1267) received from the Medical Research Council of Canada.

amino acid ester in a medium containing  $\text{NaHCO}_3$ . From the substrate specificity studies and studies involving the use of specific inhibitors of different known proteolytic enzymes Devi (7) finally succeeded to characterize the enzyme. It is, according to her findings, an enzyme very similar to chymotrypsin and has been designated as a cathepsin C like enzyme.

In recent years, several studies of the hydrolysis of proteins by proteases of various tissues have led to the discovery of more than one pH optimum, a finding generally interpreted as an indication of the presence of more than one protease (8, 9). Continuing the previous work on proteases in lens, Devi (10) recently demonstrated the presence of three pH optima, widely separated, in the pH activity curve resulted from the digestion of urea denatured hemoglobin or serum albumin by bovine lens homogenate over a pH range of 3.0 to 10.0 (Fig. 1). The variations in the ability of lens homogenate to

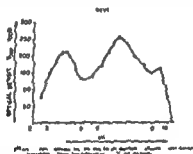


Fig. 1

hydrolyse urea denatured hemoglobin at different hydrogen ion concentrations are shown in this figure and from the three different pH optima, the author concluded that there are at least three different proteolytic enzymes in the lens, if not more. In these experiments fresh bovine lens homogenate is the source of enzymes and urea denatured hemoglobin and serum albumin were used as the substrate between pH 3.0 to 7.0 and 7.0 to 10.5 respectively. The conditions of the experiment employed in such studies are shown in Table I.

TABLE I—Experimental Conditions for the Measurement of Protease Activity of Lens Homogenate

- (1) 1.0 ml of 6.0% solution of urea denatured hemoglobin or bovine serum albumin made in 0.1 M buffer
- (2) 1.0 ml lens homogenate (70 mg ml protein/ml)
- (3) 1.0 ml buffer of 0.2 M and different pH values

Time of incubation — 2 hours

Temperature of incubation  $28^\circ\text{C} \pm 0.5^\circ\text{C}$

The enzymes were then identified by subjecting the clear supernatant fluids obtained after centrifugation at 0°C at 16 000 r.p.m. of the incubated reaction mixture to a descending chromatographic analysis. Enzymes optimally active at pH 3.8 and pH 7.0 were found to be similar to pepsin and chymotrypsin, no trypsin-like enzyme was detected, nor it was possible to identify the enzyme acted optimally around pH 8.5 to 9.0. This enzyme was not however identical with carboxypeptidase as no hydrolysis of a specific substrate for carboxypeptidase by lens homogenate was detected under the experimental conditions. The results of chromatographic analysis are illustrated in the Table II. The details of this experiment have previously been described by Devi (10).

TABLE II — Characterization of P enzymes in Bovine Lens

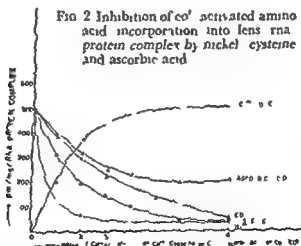
Substrates	Buffer used	pH range in which the reaction was carried out	Reagent used to develop colour of chromatograms	Colour of spot	Enzyme suspected
Carbobenzoyl L-glutamyl L-tyrosine (for pepsin)	Acetate	3.0-5.0	Ninhydrin for tyrosine	Gray bluish	Pepsin like
N-α-ethyl- tyrosine thyl esters for chymotrypsin	Phosphate	5.6-7.5	Pauly reagent for tyrosine derivatives	Orange brown with different R <sub>F</sub> values 0.9-0.2	Chymo- trypsin like
Benzyll arginine methyl ester for trypsin	Phosphate and glycyl glycine	6.0-8.0	Sakaguchi reagent for Arginine derivative	No coloured spot	No trypsin like enzyme

These findings although clearly demonstrate the importance of intracellular proteolytic enzymes (cathepsins) in maintaining the transparency of the lens do not tell us whether or not the gradual loss of proteolytic enzyme activity is caused by the inability of the lens to synthesize these enzyme proteins or is due to the denaturation of enzyme proteins. Recently Devi and associates succeeded to demonstrate the presence of an active amino acid incorporating system in rat lens (11). Based on the results derived from the *in vitro* experiments, it appears that the rat lens incorporating system is several times more active than the rat liver incorporating system of the same animal. This incorporating system is 10-12 times more active in the presence of 5  $\mu$  moles of  $\text{Co}^{++}$  than in the presence of the same amount of  $\text{Mg}^{++}$ . These results are summarized in Table III.  $\text{Co}^{++}$  can not be replaced by any other metal nor even

TABLE III — Incorporation of  $C^{14}$  Leucine into Lens RNA protein complex

Counts per minute per mg of RNA protein complex			
In presence of $Mg^{++}$		In the presence of $Co^{++}$	
Complete system	51	Complete system	49
— Mg	16	— Co	16
— ATP	12	— ATP	466
— GTP	36	+ GTP	408
+ Chloramphenicol (100 g/ml)	49	+ Chloramphenicol (100 g/ml)	478

by  $Ni$  which resembles  $Co^{++}$  in many respects  $Ni^{++}$  inhibits the incorporation of amino acids into RNA-protein complex (11, 12) Many reducing agents such as cysteine, glutathione, ascorbic acid etc have been also recently found to inhibit the incorporation of  $C^{14}$  Leucine into TCA insoluble material Addition of EDTA has been found to be equally active in suppressing the incorporation of  $C^{14}$  Leucine These results are shown in Fig 2



It has been found (13) that if the TCA precipitable material (in 5 ml of 5% TCA) is heated at  $90^{\circ}C$  for 15 mins about  $75-80\%$  of the total counts previously noted disappear which suggests that only one fourth of the total incorporated amino acid is retained by the proteins and obviously the remaining portion was incorporated into RNA Chromatographic analysis of the extract obtained by heating the TCA washed residue in  $10\%$  NaCl solution at  $100^{\circ}C$  for 30 mins,

shows that the  $C^{14}$  amino acid remained with the RNA at the origin of chromatogram which might be considered to indicate that the amino acid is truly incorporated onto the RNA. Further evidence was obtained when the NaCl extract (RNA ~aa complex) was hydrolysed in 6 N HCl and then subjected to chromatographic analysis as before. The radioactive spot was detected at the position corresponding to  $R_f$  value of free leucine used as a reference substance.

The acid insoluble material used in this experiment was obtained after centrifuging the incubation mixture to which an equal volume of 5% TCA was added. The incubation mixture contained  $5\mu$  moles of  $C^{14}$  leucine ( $0.9 \times 10^5$  c.p.m.),  $50\mu$  moles of tris buffer pH 8.5,  $2.5\mu$  moles of ATP,  $25\mu$  moles of  $Co^{++}$  and 2.5 ml of lens homogenate  $50$  mg/ml of the solution.

The Co-activated amino acid incorporating system of rat lens is truly an enzyme catalysed reaction and not merely a reaction involving RNA, amino acid and Co as in the experiment where  $C^{14}$  leucine was incubated in the presence of yeast RNA or rat liver soluble RNA and  $Co^{++}$  with and without albumin. hardly any radioactivity was picked up by the TCA precipitable material. The fact that Ni strongly inhibits the incorporation of  $C^{14}$  leucine into acid insoluble material also leads to the same conclusion. Above all a three to five fold increase in hydroxyamic acid formation occurs in Co-activated incorporating system should be considered as an additional evidence in favour of the enzymatic reaction (12).

If it is a fact that any disturbance in protein metabolism might induce the development of cataract then one would expect an abnormality in protein metabolism in ocular lenses of galactose fed rats since it is known that the feeding of a high galactose diet to young rats results in the development of cataract in their lenses (14, 15). Whether or not protein synthesis in such lenses is also affected was tested by their ability to incorporate  $C^{14}$  amino acid into RNA protein complex (16). A significant decline in the incorporation of  $C^{14}$

TABLE IV — *In vivo* incorporation of  $C^{14}$ -amino acid into lens proteins of normal and galactose fed rats

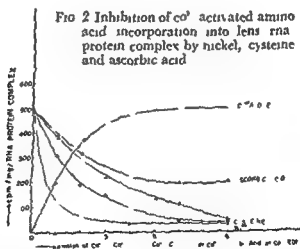
	Counts/mg of acid insoluble material			
	Normal rats		Galactose-fed rats*	
	4 hrs.	16 hrs.	4 hrs.	16 hrs.
$C^{14}$ leucine	12.4	5.0	6.0	4.3
$H^3$ valine	14.5	6.0	8.5	3.0

\* Data presented are the average of 5 such experiments. The animals were sacrificed at 4 and 16 hours after the injection of  $C^{14}$  leucine. For experimental details see the text.

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$C^{14}$ valine	14.5	6.0	8.5	3.0

\*Data presented are the average of 5 such experiments. The animals were sacrificed at 4 and 16 hours after the injection of  $C^{14}$  leucine for experimental details see the text.



into lens proteins of such animals was noted when  $C^{14}$  amino acid was administered intraperitoneally into rats 4 and 16 hours prior to death. The results are shown in Table IV. But when the incorporation experiments were carried out *in vitro* with lens homogenates of such animals in the presence of ATP,  $Co^{++}$  (or  $Mg^{++}$ ),  $C^{14}$  leucine etc. no significant reduction in the incorporation were noted as shown in the Table V. The reason for the difference in the results of these

TABLE V — *In vitro* incorporation of  $C^{14}$  amino acid into lens protein of normal and Galactose fed rats on the presence of  $Mg^{++}$  and  $Co^{++}$

	Counts/min/mg of acid insoluble material			
	Normal rat*		Galactose fed rat*	
	$Mg^{++}$	$Co^{++}$	$Mg^{++}$	$Co^{++}$
$C^{14}$ leucine	26.8	520	24.8	500
$C^{14}$ valine	18.5	610	16.8	590

\* Data presented are the average of 5 such experiments, for experimental details see the text

two types of experiments might be due to the unavailability of ATP in the former (*in vivo*) experiment and the presence of sufficient amount of ATP in the later case (*in vitro* experiments) as ATP was added externally. ATP is required for protein synthesis, without it amino acid could not be activated and as far as we know today, this is the initial step in protein synthesis (17, 18). We also know that in fully developed cataract the concentration of ATP is very low (19).

From the recent study by Devi and Puri (20) it reveals the fact that both ATP and DPN concentrations are progressively decreased with the gradual development of cataracts. Cataracts are induced by high galactose diet as well as X rays. Nearly 50 per cent of the initial ATP concentrations appears to be lost with a visible sign of lenticular opacity (observed under biomicroscopy). The decrease in ATP concentrations is further progressed with the extension of opacification and finally a complete disappearance in fully matured cataract is observed. Lens is apparently devoid of ATPase activity with the exception of that in a very superficial layer of epithelial cells. The disappearance of ATP during the development of cataract appears to be due to the impairment of synthesis of ATP itself since no appreciable increase in ATPase activity has been detected in the cataract. That ATP generating system in the lens of rats with high galactose diet is seriously disturbed, has also been noted from recent investigation (21). It is to be noted here that a complete disappearance of ATP in all types of senile cataract supports the view that an interference of protein synthesis during progressive development of cataract occurs. High energy phosphate bond is indispensable for activating amino acids before the peptide chain is synthesised on a RNA template.

The unavailability of ATP in galactose induced cataracts seems to be therefore the real cause of decreased protein synthesis

### PROTEOLYTIC ACTIVITY OF CATARACTOUS LENS

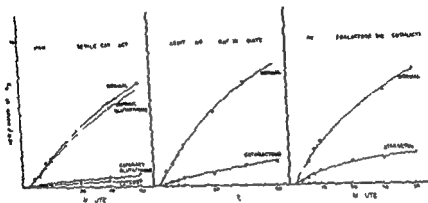


Fig 3

Do we also find a concomitant loss of proteolytic activity in galactose induced cataracts? In order to know this the determination of proteolytic activity of the lenses of such animals was undertaken. A progressive loss in proteolytic activity was noted during the gradual development of cataract in fact a loss of 70-90 per cent activity was found in fully developed cataracts in senile cataract and cataracts induced by either  $\lambda$  rays or by feeding diets containing galactose as shown in Fig 3

Thus a complete loss of proteolytic activity in the fully developed cataracts is observed in all cases as shown in this figure. It does not matter how it is caused.

Although it appears that the loss of proteolytic activity is the real cause in the development of cataract nothing is known why the activity is progressively lost during the development of cataract. Is it due to the impairment of protein synthesis in the lens resulting in the decrease of the protease concentration that is not known. We do however know that the ATP concentration is greatly reduced which might interfere with protein synthesis. In any case it appears that the development of cataract in one way or other is caused by a defect or defects in protein metabolism possibly in protein synthesis and more precisely in the synthesis of enzyme (proteolytic) proteins. It is not the end of the work rather appears to be the beginning of our research for the primary cause which interferes with the mechanism of protein synthesis. Our laboratory is actively engaged in such work. The knowledge we expect to gain through researches will be of immense value in preventing and curing this disease.

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# L'IMPORTANCE PRATIQUE DE L'EXAMEN DE LA FONCTION VÉGÉTATIVE DE LA RETINE

M. RADNÓT ET E. WALLNER

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La lumière provoque une eosinopénie sur l'individu normal. C'est ce qui se reflète dans le sang par l'oscillation journalière des cellules éosinophiles. Si ces mêmes individus sont soumis à l'obscurité, le nombre des cellules éosinophiles reste invariable (1). L'intensité de l'eosinopénie causée par la lumière s'approche de celle observée à l'épreuve de Thorn à la suite de l'application de l'adrénaline ou de l'ACTH. Le fait mentionné ci-dessus peut être attribué à l'activité du système hypophyso-surrénal et peut être enregistré comme une manifestation de la fonction optico-végétative.

Au point de vue théorique et clinique il y a intérêt à examiner quelles maladies de l'œil peuvent influencer l'effet de la lumière de l'eosinopénie normale. Nous avons pu établir dans le matériel examiné que les opacités de la lentille et du vitre n'y exercent aucune influence même si l'acuité visuelle baisse considérablement. En cas de dégénération pigmentaire de la rétine aussi, là où le rétrécissement concentrique du champ visuel s'est réduit à 5-10°, la lumière provoque une eosinopénie normale. Par contre le centre de la rétine intacte est la condition primordiale de l'effet végétatif de la lumière. En cas d'une dégénération de la macule, là où la périphérie se trouve intacte mais le centre comporte des altérations, l'effet de la lumière ne provoque pas d'eosinopénie.

Dans ce dernier groupe chez la majorité des malades on a pu observer à l'aide de l'ophtalmoscope des altérations profondes comportant une baisse remarquable de l'acuité visuelle et un scotome central très étendu. Mais dans bien des cas les altérations du fond de l'œil étaient minimes, le scotome central peu réduit (5°) ou bien on n'a pu observer qu'un scotome relatif de couleur bleue. L'acuité visuelle peu réduite (5(10-5)25) le nombre des cellules éosinophiles n'a cependant point montré d'altération sous l'effet de la lumière (2). Cette observation est d'autant plus remarquable que dans les cas d'inflammation rétrobulbaire du nerf optique même à un scotome central absolu et très étendu et à une baisse remarquable de la vision (1° M à la lecture au doigt) le processus n'a pas empêché non plus l'apparition normale de l'eosinopénie causée par la lumière (3).

Selon nos examens nous pouvons donc considérer comme point de départ de la fonction optique végétative une partie centrale peu

étendue mais bien décrite de la rétine. La voie optique se comporte autrement que celle qui est purement optique, c'est pourquoi la voie optique et la voie optico-vegetative doivent être séparées l'une de l'autre non pas tant au point de vue anatomique mais plutôt au point de vue fonctionnel.

L'examen de l'éosinophilie, causée par la lumière, peut également fournir des résultats utiles dans la pratique ophtalmologique. En cas d'opacité de la cornée lorsque l'emploi de l'ophtalmoscopie est inexécutable on peut constater de telle façon quel est l'état du centre de la rétine, vaut-il la peine de soumettre le malade à une opération, par ex. peut-on s'attendre à une bonne guérison visuelle à la suite de l'opération de la cataracte. Une cataracte bien développée mais en présence d'une rétine saine provoque en effet une réaction d'éosinophilie, tandis qu'elle est éliminée en cas d'une dégénération de la rétine qui se dissimule derrière la cataracte.

L'examen de l'éosinophilie dans la période initiale d'une maladie peut servir à confirmer le diagnostic. Dans un de nos cas l'examen d'un homme relativement jeune a révélé une altération du fond de l'œil à peine appréciable, un scotome central très réduit et une baisse relative de la vision. Le soupçon de l'aggravation a été dissipé par ce fait que l'éosinophilie n'a pas eu lieu sous l'action de la lumière.

Parmi les amblyopes de l'enfance il y a un groupe spécial de tels cas où la cause des amblyopies se trouve dans la rétine. Il ne vaut pas la peine de les exposer à des traitements épuisants et superflus. Leur isolement est possible par ce fait que nous ne provoquons pas de réaction d'éosinophilie sous l'action de la lumière (1).

En ophtalmologie le nombre de tels examens est relativement réduit qui s'appuient sur le jugement objectif du malade. L'introduction de l'examen de l'éosinophilie en diagnostic pourrait signifier un tel procédé objectif.

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# ARTERIOSCLEROTIC RETINAL VASCULAR CHANGES WITH AGING PROCESS IN HYPERTENSION

TETSUO IIZUKA

Ji kei University, School of Medicine, *Tokyo, Japan*

(Director Prof. K. OHASHI)

I have studied on the changes of ocular fundus in hypertensive patients and have already reported the scoring method to evaluate the degrees of arteriosclerosis in retinal vessels

I concluded in my previous Japan report that the crossing signs were most important to diagnose the hypertensive ocular fundus in adult

But in older persons their fundus changes were very different from that of adult and sometimes it seemed difficult to determine the diagnosis of arteriosclerosis due to aging process on the retinal vessels

Therefore I wanted to find a rule to diagnose and classify the arteriosclerotic fundus changes throughout every generation and conducting a research at this time on every vascular change in hypertensive patients

As a first step of my study the following results of the examination ages from 20 to 70 patients totalling 340 patients

I measured their systemic blood pressure, retinal blood pressure and checked every changes in ocular fundus vessels such as vascular reflex narrowing of vascular lumen irregularity of vessel calibres opacities of vessel walls Gust's phenomena and crossing signs Also I took a fundus photograph for recording

The results are as follows

- 1) Vascular reflex (Table 1)  
Table 1 shows a rate of vascular reflex in each generation
- ) Normal vascular reflex most frequently in 20 and 30  
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L'examen de l'eosinopenie, causee par la lumiere, peut egalement fournir des resultats utiles dans la pratique ophtalmologique. En cas d'opacite de la cornee lorsque l'emploi de l'ophtalmoscopie est inexecutable on peut constater de telle facon quel est l'etat du centre de la retine, tout il la peine de soumettre le malade a une operation, par ex. peut on s'attendre a une bonne vue visuelle a la suite de l'operation de la cataracte. Une cataracte bien developpee mais en presence d'une retine intacte provoque en effet une reaction d'eosinopenie, tandis qu'elle est eliminee en cas d'une degeneration de la retine qui se dissimule derriere la cataracte.

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Table 2 shows a degree and rate of the narrowing
- (-) Normal vessel lumens highest in 20  
After that gradually decreased until 70

Table 1

1 vascular reflex

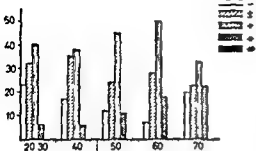


Table 2

2 caliber narrowing

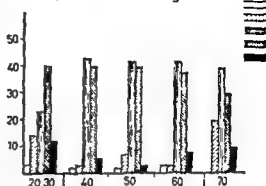


Table 3

3 caliber irregularity

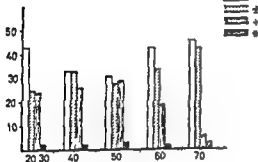


Table 4

4 vascular wall opacity

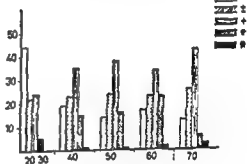


Table 5

5 guists phenomenon

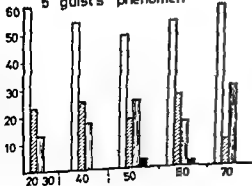
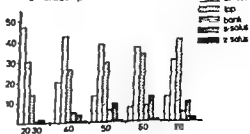


Table 6

6 cross phenomenon



- (±) Highest occurrence at 40 after that almost no changes until 60  
In 70 rapid increase
- (+) In 20 lowest, in 40 rapid increase, after that, until 70 no changes
- (++) In 20 and 40 highest occurrence, after that gradual slight decrease until 70
- (3) Irregularity of vessel calibres (Table 3)
- (-) Normal calibre, in 20 irregularity highest occurrence in 40 and 50 decreased in 60 and 70 increased again
- (±) In 20 and 40 slightly increased, in 50 decreased  
After that in 60 and 70 increased again
- (+) From 20 to 50 increased but in 60 and 70 decreased
- (++) No changes between each generation
- (4) Opacities of vessel walls (Table 4)
- (-) Vascular walls without any opacities highest at 20 until 50 rapidly decreased but no changes in 60 and 70
- (±) From 20 to 70 slightly increased
- (+) Until 50 relatively rapid increase in 60 same as in 50 in 70 increase again
- (++) Until 60 slowly increased in 70 slightly decreased
- (+++ ) From 20 to 70 gradually increased
- (5) Guist's phenomena (Table 5)
- Table 5 shows a rate and degree of Guist's phenomena in retinal vessels
- (-) Negative Guist's phenomena most frequently seen in 20 until 50 gradually decreased after that slightly increased
- (±) In 20 and 40 increased  
in 50 decreased  
in 60 increased again  
in 70 decreased again
- (+) Until 50 increased,  
in 60 decreased  
in 70 increased again
- (+++ ) No changes between 20 to 40,  
in 50 rapid increase,  
in 60 decreased  
in 70 same as in 60
- (6) Crossing signs (Table 6)
- Table 6 shows a frequency of crossing signs in each type
- (-) Negative pathological crossing signs highest in 20 until 60 rapid decrease but in 70 same as in 60

- (i) Concealment  
From 20 to 40, rapid increase,  
after that gradual decrease until 70
- (ii) Tapering  
From 20 to 70 slightly increased
- (iii) Banking  
From 20 to 60, increased,  
in 70 slightly decreased
- (iv) S Salus  
Almost same as Banking
- (v) Z Salus  
Found at 40 in the first, after that  
in 50 slightly increased,  
in 60 and 70, same as in 50

From these results, a difference could not be discovered of each generation. Therefore, I executed a scoring method on all patients and discovered the following

According to the degree separations were made from 1-4 (Table 7)

Total score of each patient would mean the degree of arteriosclerosis

Results were as follows (Table 8)

- (1) Score of crossing signs  
in 20 showing lowest score,  
in 50 highest score,  
in 70 lower than that of 50

Table 7

## 7 scoring

scoring		1	2	3	4
art reflex		±	+	++	+++
calb narrow		±	+	++	+++
calb irreg		±	+	++	+++
wall opacit		±	+	++	+++
guist phen		±	+	++	+++
cross phen	conceal	o			
	arch	o			
	tap		o		
	bank			o	
	s salus	o			
	z salus		o		

Table 8

## 8 average score of vascular changes

age	cross signs	vascul signs	total signs
20-30	10	49	59
40	18	69	87
50	26	74	100
60	25	72	97
70	20	73	93

- (2) Score of other signs except crossing signs
  - in 20 showing lowest score,
  - in 50 highest one,
  - in 60 and 70 almost same as in 50
- (3) Total score of all signs
  - in 20 lowest
  - in 50 highest,
  - in 60 and 70 almost same as in 50

From these results the crossing signs should be very valuable for diagnosis of hypertensive fundus changes in younger patients under 60 years of age as previously reported

But in older patients especially over 70 years of age that is not so valuable as in younger age. Depending only on crossing signs evaluation at times be erroneous

I would like to stress from my research that we must emphasize for diagnosis of hypertensive fundus changes not only by crossing signs but also by other changes of retinal vessels

For this purpose my scoring method would be the most useful guidance to evaluate the fundus hypertension

- (i) Concealment  
From 20 to 10, rapid increase,  
after that gradual decrease until 70
- (ii) Tapering  
From 20 to 70 slightly increased
- (iii) Banking  
From 20 to 60, increased,  
in 70 slightly decreased
- (iv) S Salus  
Almost same as Banking
- (v) Z Salus  
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Total score of each patient would mean the degree of arteriosclerosis

Results were as follows (Table 8)

- (1) Score of crossing signs  
in 20 showing lowest score,  
in 50 highest score,  
in 70 lower than that of 50

Table 7

## 7 scoring

scoring		1	2	3	4
art reflex		±	+	++	+++
calb narrow		±	+	++	+++
calb irreg		±	+	++	+++
wall opacit		±	+	++	+++
guist phen		±	+	++	+++
cross phen	conceal	o			
	arch	o			
	tap		o		
	bank			o	
	s salus	o			
	z salus		o		

Table 8

## 8 average score of vascular changes

age	cross signs	vascul signs	total signs
20-30	10	49	59
40	18	69	87
50	26	74	100
60	25	72	97
70	20	73	93

Yet contrary to such an anatomical and structural uniformity relating to the eye and its parts, no less impressive information presents a quite dissentient behaviour of the vasculous formations which occur in the vitreo retinal block which in opposition to the persistent uniformity manifested by all other parts display in that space an utmost variability.

From what has been stated above one must fairly easily reach the conclusion that the actual subject in dispute of the matter under consideration does factually consist not only in reasons that, on the one hand call for such a firmly retained uniformity of the greater part of the eye through the entire differentiation of these animals and on the other claim for such an impressive and peculiar variability of the circulatory system in the vitreo retinal space represented by the vasculous formations as exactly are the hyaloid circulation in fishes and amphibians the *corus vasculosus* (papillaris) in reptilians, the pecten in avians and the direct vascularization of the retina in mammals but also in reasons which call for such a tenacious retention of an inverted constitution of the retina of these eye.

It stands to reason that the anatomical and histological uniformity of the eye and its parts rests upon biooptical grounds in connection with the functioning of this organ which physically conceived *procre* to be in their essentials very close in all classes of these animals. On the contrary, the opposite phenomenon, the one of the extraordinary variability which occurs in the optical space *sensu strictiori* cannot be of such a kind in nature for the reason that even the mere presence of a circulatory system in that portion of the eye presents a non transparent obstacle that impinges with the course of the light rays towards photoreceptors i.e. with the appropriate agent of this organ toward its actual goal and so absolutely *interferes* with its functioning.

In line with this it is also an obvious fact that the other of the considered phenomena the inverted constitution of the retina represents less favourable a state as regards its functioning than does in fact afford its opposite for the simple reason that through such a state the quantity of light energy before having reached the photoreceptors is reduced a good deal by absorption of the retinal troma and actually interferes with the functioning of this organ.

Here it is therefore pertinent to state that it was possible to reach further conclusions of a predominant importance as a result of a subsequent analytical work on this subject.

Firstly that the actual shape and location of the vasculous formations in the vitreo retinal space are eminently dependent on the mode of subsistence that a definite group of these organisms is managing.

Secondly that the inverted constitution of the retina is proved to be a result of an activity that takes place on its surfaces.



# MATHEMATICAL CONCEPTION OF THE DYNAMICAL PHENOMENON IN RESPONSE TO WHICH THE RETINA ASSUMED AN INVERTED CONSTITUTION

MLADEN SEBASTIAN, M D (*Zagreb, Yugoslavia*)

The problem in question arose from the study of the physiological meaning of some apparent but rather peculiar morphological phenomena which occur in the organ of sight in living organisms the body of which is supported by a vertebral column

In that respect, the present discussion is an outgrowth of studies on morphology of the eye in vertebrata given by the author in a monograph published in 1960 \*

Its aim is to cover the morphological data with mathematically conceived physiokinetic instruments

The subject, we should like to start with, constitutes two most important, though familiar, statements established on an almost superficial approach to the matter involved

The one that states that the uniformity of this organ does truly figure as one of the most impressive phenomena throughout all classes of these organisms, irrespective of the mode of activity that they live, i.e., from their lowest still living aquatic forms as exemplified by cyclostomes, up to Man, the highest living organism endowed with a bony skeleton

The second that says that all representatives of this large and prominent group of living organisms, in contrast to all others, proved to possess an inverted constitution of their retina

The first of these statements does not really refer only to the form of that organ and the parts of it, but is just so strictly true of its general anatomical make up, the spatial interrelations and the structures of its parts

In this respect, it should be emphasized that the uniformity of the eye in vertebrata does not only by far surpass the one of all the other parts of their body whenever such a phenomenon can be observed but that it does even outtop the plainly conspicuous uniformity manifested by the bony skeleton, in accordance with which that group of organisms has been denominated

(\*) Mladen Sebastian THE PROBLEM OF INVERTEDITY OF THE RETINA IN MAN AND THE ASSOCIATED PROBLEMS

Znanstveni dopisnici Jugoslavenske Akademije ZAGREB YUGOSLAVIA

Yet, contrary to such an anatomical and structural uniformity relating to the eye and its parts no less impressive information presents a quite dissentient behaviour of the vasculous formations which occur in the vitreo-retinal block which in opposition to the persistent uniformity manifested by all other parts display in that space an utmost variability.

From what has been stated above one must fairly easily reach the conclusion that the actual subject in dispute of the matter under consideration does factually consist not only in reasons that on the one hand call for such a firmly retained uniformity of the greater part of the eye through the entire differentiation of these animals and on the other claim for such an impressive and peculiar variability of the circulatory system in the vitreo retinal space, represented by the vasculous formations as exactly are the hyaloid circulation in fishes and amphibians the *conus vasculosus* (*papillaris*) in reptilians, the *ecten* in avians and the direct vascularization of the retina in mammaliars but also in reasons which call for such a tenacious retention of an inverted constitution of the retina of their eye.

It stands to reason that the anatomical and histological uniformity of the eye and its parts rests upon biooptical grounds in connection with the functioning of this organ which physically conceived prove to be in their essentials very close in all classes of these animals. On the contrary the opposite phenomenon the one of the extraordinary variability which occurs in the optical space *sensu strictiori*, cannot be of such a kind in nature for the reason that even the mere presence of a circulatory system in that portion of the eye presents a non transparent obstacle that impinges with the course of the light rays towards photoreceptors i.e. with the appropriate agent of this organ toward its actual goal and so absolutely interferes with its functioning.

In line with this it is also an obvious fact that the other of the considered phenomena the inverted constitution of the retina, represents less favourable a state as regards its functioning than does in fact afford its opposite for the simple reason that through such a state the quantity of light energy before having reached the photoreceptors is reduced a good deal by absorption of the retinal stroma and actually interferes with the functioning of this organ.

Here it is therefore pertinent to state that it was possible to reach further conclusions of a predominant importance as a result of a subsequent analytical work on this subject.

Firstly, that the actual shape and location of the vasculous formations in the vitreo-retinal space are eminently dependent on the mode of subsistence that a definite group of these organisms is managing.

Secondly, that the inverted constitution of the retina is proved to be a result of an activity that takes place on its surfaces.

Furthermore, conclusive evidence has been provided that the phenomena being in point in either instance become produced by one and the same factor proved to be in the aquatic life the mode of motion and in the aerial one the activity of the heart

That is to say that the listed phenomena become produced in the first instance by undulating movements of the body, and in the second, the pulse of haemodynamics, and that there actually exists a reciprocal relationship between the motion in the aquatic life and the haemodynamics in the aerial one in the range of biophysics

In view of these facts it is of no neglectable importance to state here that this factor in either mode of life from the standpoint of biomechanics can easily be resolved into two components

In the pressoric one, which is produced in the aquatic life hydrodynamically on the external surfaces of the eye, and in the aerial one, haemodynamically inside the vitreo retinal block

Speaking in terms of mathematics, its ratio is given in the first instance, by the equation of Bernoulli, and in the second, by the extent of the amplitude of the pulse of the blood pressure inside that block, which means the space encompassed by Bruch's membrane

The other component, being a consequence of the principle of inertia, is produced in the aquatic life by undulating deflections of the eye masses to right and left from the direction of advance, and in the aerial one, by displacements of the eye masses through the pulsation of the lumen of the uterus

Mathematically expressed, the ratio of these components is given in either instance by the greatness of the impulse, i.e. the product of velocity multiplied by mass

Physically conceived, either component, being responsible for the listed phenomena, represents forces brought about in the first instance by the strain of the substance that the vitreo retinal block is built of, and in the second, by making active the masses of this portion of the eye

Of a particular interest is the fact that the very nature of these forces is such as to give no rise to effects of whatsoever physiokinetic activity as long as they occur in a homogeneous or, physically expressed, a continuous and isotropic medium. But the vitreo retinal block presents a continuous and isotropic medium only up to the limit between the vitreous humour and the stroma of the retina or, speaking in words of physico chemistry, up to the interface between both portions of this block

Consequently, in that interface does exactly occur not only a mechanical discontinuance of the vitreo retinal block, but there also occurs a contact between two substances with plainly different physical properties

On the basis of these analytical remarks and data one is authorized to state here that it is a well established fact that a disturbance of any

kind in our case the first component of the factor represented by the compressional wave propagating in one medium and impinging upon an interface gives rise not only in general to reflected and refracted waves but also to a series of subsequent physiokinetic effects because of an interfacial sliding and friction between surfaces of the both fairly liquid but living substances being here in contact as well as to dissipation of heat, according to the first fundamental law of thermodynamics due to friction in that place and the second fundamental law of thermodynamics due to the transformation of the impulse that occurs in that place

It is further true that the second component of this factor, the activity of the masses made active by motion according to the principle of inertia engenders in the interface, representing a mechanical discontinuance, successive effects in response to different modes of vibration they become involved in *en bloc*, owing to different physical properties possessed by either portion of the vitreo-retinal block being in contact

The physiokinetic effects of the second component are found to be the same in nature as the ones of the first component but far more expressed

Speaking in terms of mathematics they represent periodic but unharmonic vibration the ratio of which is covered by the Fourier's theorem

Here it is therefore proper to state that from the standpoint of physiokinetics either component engenders effects on the retinal surfaces which substantialize inadequate influences to the retinal tissue but the more so to its specific sensory cell elements and which are proved to be disturbing and harmful to the functioning of the eye

From the discussion which has been given above it must be evident firstly, that the inverted constitution of the retina substantializes a protective disposition in particular for the photoreceptors because these extremely sensitive cell elements become by inversion merged in the mechanical homogeneity of the choroiretina, and secondly, that the vasculous formations in the vitreo-retinal block, with their shape and location substantialize special self protecting forms of the circulatory system well matched with the mechanical influences that their haemodynamics in a given case is involved in

# RETINOBLASTOMA IN THE ADULT REVIEW OF LITERATURE AND REPORT OF CASE ASSOCIATED WITH A BENIGN MELANOMA

JOHN R. FINLAY, M.D.  
HERVE BYRON, M.D.

To date only four retinoblastomas in the adult have been reported in the ophthalmic literature. The rarity of such a tumor warrants the presentation of any new case. This is the first of a retinoblastoma in a senile patient in which, simultaneously, there is a melanoma.

The documentation of primary neuroepiblastic tumors has long been confused by the dispute in terminology. In 1861 v. Graefe thought that the tumor represented a sarcomatous hyperplasia of the retina. Two years later Virchow postulated that these tumors arose from glial cells of the retina and were therefore comparable to gliomas of the brain. Flewener suggested the term neuroepithelioma in 1891 because of the presence of rosettes of epithelial cells. Six years later, Wintersteiner adopted this term although it was not universally accepted. In 1918 Fisher proposed the term neuroblastoma in view of the embryonic character of the growth. Verhoeff suggested the name of retinoblastoma in 1924 for those malignant tumors originating from the neural cells of the retina. He advocated reserving the name glioma for only those tumors which were true astrocytomas, e.g. derived from the supporting structure of the retina and NOT from the neural elements. The name was officially adopted by the American Ophthalmological Society in 1926. Bailey and Cushing in the same year formulated a new classification for brain tumors into three cells based on the differentiation of the medullary epithelium lining the neural tube.

- |                |                                   |
|----------------|-----------------------------------|
| 1 Neuroblast   | Neuronal cells                    |
| 2 Spongioblast | mostly astrocytes ependymal cells |
| 3 Medulloblast | glial cells neuronal cells        |

This served as a basis for Duke Elder's classification which considered the retinoblastoma as one of five types of primary neuroepiblastic tumors.

1 RETINOBLASTOMA — malignant tumor arising in early youth, usually from the posterior part of the retina, composed of primitive cells, retinoblast, which are analogous to the medulloblast of the central nervous system. These cells are small, closely packed, round or polygonal with large darkly staining nuclei and scant cytoplasm and appear extremely undifferentiated or uniphasic.

2 **NEUROEPITHELIOMA** — malignant tumor arising from the external or internal nuclear layer of the retina, composed of primitive spongioblasts which are the same cells in the central nervous system and which manifest rosette formation. This rosette formation rarely predominates in the overall histology of this tumor. They are thought to indicate a somewhat slower growing and therefore less malignant neoplasm than the retinoblastoma. The cytology in this tumor is more differentiated than the retinoblastoma.

3 **MEDULLOEPITHELIOMA** — malignant tumor arising from the ciliary epithelium in the eye which in turn develops from the primitive retinal epithelium of the medullary epithelium of the neural tube of the brain. These tumors are very rare. In the infant it is manifest as a diktyoma. In the adult it may develop from malignant degeneration of pigment epithelium.

4 **NEUROBLASTOMA OR NEUROCYTOMA** — these tumors stem from neuroblasts and are characterized by a high degree of differentiation.

5 **ASTROCYTOMA** — a tumor arising from true glial tissue. It is the most common brain tumor, but is very rare in the eye.

The term retinoblastoma as recognized by American ophthalmologists includes both the neuroepithelioma and retinoblastoma of Duke Elder's classification.

Verhoeff postulated that two distinctly different types of retinoblastomas exist. The first type is congenital in origin or develops from some congenital anlage. Tumors of this type rarely manifest themselves later in life. The second type arises late in life from cells which were originally normal. Our case report falls into the second category.

Reese feels that the tumor arises from primitive retinal epithelium. In his classic book on tumors of the eyes, he cites Parkhill and Benedict's belief that most of these tumors arise from the inner retinal layers. Since glial cells predominate in this layer, they use this as an argument that the most probable origin of retinal tumors is the dedifferentiation of these glial cells. Reese vitates this theory by noting the difficulty of trying to ascertain which specific layer of the retina the tumor originates.

### Report of Case

#### HISTORY

M.D.P. white female age 74 years was first seen by Brittain F. Payne M.D. on April 6, 1955, complaining of acute pain in the right eye. She stated that vision had been lost without pain six months earlier. Examination revealed a hard globe, corneal edema, shallow anterior chamber and no light perception. The fundus was not visible. A diagnosis of absolute glaucoma was made but the presence of an intra-ocular tumor was discounted on the basis of a normal transillumination. Bilateral nuclear cataracts were present. Vision in the left eye was correctable to 20/50.

## GENERAL DESCRIPTION OF GLOBE

Horizontal sections of the prepared globe were of normal size and shape, measuring 24 x 21 mm (AP x horizontal). The retina showed thickening and deep basophilic staining and complete detachment by a sub retinal protein precipitate. Posteriorly, the growth was limited by the lamina cribrosa but in this area there was extension to the adjacent choroid. The iris showed loss of crypts and folds. There was a basophilic thickening centrally and peripherally, it showed broad peripheral anterior synechiae. The lens was sclerosed. On the nasal side there was a fusiform pigmented tumor of the pars plana of the ciliary body.

## MICROSCOPIC DESCRIPTION

**CORNEA** The cornea was not remarkable. There was no evident microcystic edema. Peripherally there was some vascular engorgement. Posteriorly and temporally in the area of the pseudo angle there was a membrane of tumor cells which covered the endothelium.

**LIMBUS** The epithelium was normal. The sub epithelial tissue showed some vascular engorgement and perivascular round cell infiltration. The stroma showed tumor infiltration into the collecting vessels. The chamber angle was closed by PAS on both sides. The pseudo angle was covered by a neoplastic membrane. The trabecular meshwork was compressed and Schlemm's canal was filled with cellular debris, pigment and tumor cells.

**SCLERA** The sclera was not remarkable. Nasally, 2 mm from the limbus, there was a nerve loop of Axenfeld.

**LAMINA CRIBROSA** The lamina cribrosa was of normal contour. The tumor growth had not infiltrated posteriorly into the nerve.

**IRIS** The iris was atrophic. There was loss of the crypts and folds and posterior fistoonations. There were broad PAS. Anteriorly there was a dense neoplastic membrane which had produced an ectropion area. Small round cells had invaded the stroma in focal fashion anterior to the sphincter muscle. Elsewhere the stroma was replaced with fibrous tissue.

**CILIARY BODY** The ciliary body showed similar atrophy. On the nasal side in the area of the pars plana there was a fusiform densely pigmented tumor 3 x 5 mm in length. Posteriorly it involved the long ciliary nerve to the equator and anteriorly to 1 mm from the nerve loop of Axenfeld. Depigmented sections showed the tumor composed of spindle cells densely filled with melanin pigment granules, long fusiform nuclei, abundant cytoplasm with tapered ends arranged in parallel bundles. This growth represented a benign Schwannian melanoma.

**CHOROID** The choroid was unremarkable. There was slight atrophy and diffuse round cell infiltration. The lamina vitrea was

apparently intact and had resisted the spread of the tumor into the choroid. However, where it was absent about the optic disc the tumor had spread about the intermediate tissue of Kuhnt into the choroid largely on the nasal side for 1 mm.

**RETINA** The retina was detached from the ora to the optic disc. It was thickened most markedly posteriorly, disorganized and almost entirely replaced by neoplastic cells. These cells were seen to arise from the inner nuclear layer. They showed a perivascular arrangement which had been termed pseudo rosettes. The tumor had broken the internal limiting membrane posteriorly and had spread into the vitreous cavity. Externally, it had spread through the external limiting membrane and had diffusely spread into the subretinal serous fluid. It had penetrated beneath the pigment epithelium and had formed a dissecting membrane between Bruch's membrane and the pigment epithelium.

The subretinal space was filled with free floating tumor cells, red cells and macrophages. The tumor was composed of large densely arranged round and polyhedral cells having large nuclei with well defined nucleolar walls. They were rather pale with coarse clumping of the nuclear chromatin. The cytoplasm was scarce and poorly staining, showing almost bare nuclei. Mitotic figures were frequent. There was no calcium present. However, areas of marked karyolysis and pyknosis suggested early necrosis.

**ANTERIOR CHAMBER** The anterior chamber was decreased in depth and diameter by peripheral anterior synechia. It was filled with protein precipitate.

**LENS** The lens capsule was intact. The subcapsular epithelium was normal. There was some liquefaction degeneration of the cortex. The nucleus was sclerosed.

**OPTIC PAPILLA** The optic papilla was replaced by tumor tissue which extended to the lamina cribrosa.

**OPTIC NERVE** The optic nerve showed no tumor invasion in the sections studied.

#### OPHTHALMOLOGY PATHOLOGY DIAGNOSIS

- Retinoblastoma right eye
- Glaucoma secondary
- Benign Schwannian melanoma
- Retinal detachment solid
- Tumor invasion of choroid
- Tumor implantation on iris

#### CLINICAL COURSE

The slides were reviewed by many outstanding ophthalmic pathologists April, 1956, who concurred with the diagnosis.



Dr. Verhoeff commented at the time that with such typical spread of the retinoblastoma to the choroid he had not seen a case survive more than a year.

May 12, 1956 The patient was admitted to Jacobi Hospital with right hemiplegia and motor spasm of four weeks duration. Craniotomy was performed for intra cranial space taking lesion. Biopsy of a frontoparietal lesion was taken. The patient died July 27, 1956, and autopsy was performed at Jacobi Hospital.

#### SUMMARY OF AUTOPSY FINDINGS

**BRAIN** "The tumor occupying the left frontoparietal region measured about 10 cm in diameter which was adherent to the dura. There was no evidence of herniation. The right optic nerve was smaller than the left. Sections of the adjacent pons, basal ganglia, and cerebellum showed many foci of perivascular infiltrates.

The meninges over the main lesion showed slight to moderate degree of monocytic infiltration with some lymphocytes.

- |             |  |
|-------------|--|
| Primary     | 1 Tumor, left frontoparietal lobe                          |
|             | 2 Remote status — Post operative craniotomy                |
| Secondarily | 1 Cholelithiasis   |
|             | 2 Chronic passive congestion and fatty infiltrate of liver |
|             | 3 Right pleural adhesion                                   |
|             | 4 Remote enucleation, right eye                            |

Microscopic sections taken from the central area of the tumor showed an infiltrating lesion composed of highly cellular elements. The cells were round, oval or polygonal and uniform in size. There was scant cytoplasm with almost naked nuclei. The nuclei had prominent walls and coarse clumping of chromatin. Mitotic figures were infrequent. The cells were loosely arranged with little stroma. The tumor was not highly vascular. However, in the periphery there was perivascular infiltrates of cells. The cells showed even distribution, were well preserved and no areas of necrosis or calcification were seen. (Photo 10 × 11-12)

The cytologic identity of the retinal and cerebral tumor was unmistakable" (See Figures 9 and 11)

#### REVIEW OF LITERATURE

Verhoeff published the first American report of a retinoblastoma in an adult in 1929. In his paper he mentioned Wintersteiner's documentation in 1897 of 167 patients manifesting this tumor, the oldest of which was sixteen years old. He also cited Margby's report in 1919 of a patient who had a glioma retinae in her right eye at the age of two years. When her left eye was enucleated at the age of twenty years

because of glaucoma, it was found to contain a large retinoblastoma. This patient was the oldest to harbor this tumor before Verhoeff reported his case. In his paper Verhoeff cited two case reports of Gerard and Detroy, and Gerard and Morel in which a sixty six year old female and thirty five year old male presumably manifested this tumor. He doubted the validity of these reports because of their brief pathologic descriptions and lack of photomicrographs. A summary of Verhoeff's case report is as follows:

A forty eight year old white male was admitted to the Massachusetts Eye and Ear Infirmary because during an examination one week before he had noticed that the sight in his left eye was almost gone. This was unaccompanied by pain but he did have a feeling of numbness on the left side of the head.

Examination of his eyes revealed a normal right eye. The only abnormalities noticed in the examination of his left eye were a moderate number of cells in the A. C., dilatation of the iris vessels, poor reaction of the pupil to light, posterior synechiae at 7 o'clock, posterior cortical cataract and a vitreous full of fine opacities.

There was a circumscribed separation of the retina on the nasal side anteriorly. The projection was irregular in contour and its surface showed prominent blood vessels. It transilluminated fairly well but irregularly. The tension was 24 mm. The vision in his left eye was finger counting at two feet.

The left eye was enucleated on the day of admission with a clinical diagnosis of intraocular neoplasm. The patient was seen seven months later at which time his general health was found to be excellent.

The globe was of normal size and shape on macroscopic examination. In the upper nasal quadrant there was a large, greyish white intraocular tumor which extended from the root of the iris to a point 3 mm. from the optic disc and from the vertical meridian above to slightly below the horizontal meridian.

Microscopic examination showed that the anterior portion of the growth was situated within and greatly distended the ciliary body, anterior choroid and suprachoroidal space. The inner layers of the choroid and ciliary body and ciliary processes were relatively intact and formed a covering for the tumor. There was, however, a gap 3 to 5 mm. wide beginning 8 mm. from the filtration angle where the uvea had been broken through by the tumor which here attained its greatest thickness.

The parenchyma of the tumor consisted almost exclusively of rosettes of various sizes identical in appearance with those of a retinoblastoma. Bordering the lumen of each rosette was a membrane analogous to the external limiting membrane of the retina but the cells did not project through this membrane.

Occasionally the appearance of a fairly long irregular tubule was produced entirely due to the compression of a large rosette.

by the surrounding cells. Rows of cells representing parts of walls of rosettes were often seen. Many of these had obviously resulted from the invasion of rosettes by the neighboring cells. Cells in mitosis were abundant throughout the tumor.

The stroma of the tumor was scant. There was no reticulum between the tumor cells. Within the tumor there were numerous areas of necrosis. Some of them were replaced by connective tissue. Within the areas of necrosis there were frequently seen sharply defined circular areas of tumor cells, each area containing a central vessel. These were really cylindric formations seen in cross sections, such as described and explained by Wintersteiner.

Microscopic examination of the other parts of the eye showed nothing of special importance, aside from changes confirming the age of the patient. Several beautiful photographs accompanied this article.

The second authentic retinoblastoma in an adult was reported by McCrea in 1913. A summary of his case report is as follows:

A 67 year old male was treated by an ophthalmologist for several years conservatively for cataracts of both eyes. On March 1, 1937, an intracapsular extraction with complete iridectomy was performed on the right eye uneventfully. At that time the left eye showed incipient cataract changes, fine vitreous floaters and a corrected visual acuity of 6/25. On February 26, 1942, his left eye revealed a cataractous lens with inaccurate light projection, a tension of 23 mm. A week later a combined complete iridectomy and intracapsular extraction of the left eye was performed.

A membrane was seen in the vitreous at that time. The eye remained red and painful despite treatment of NAB, sodium salicylate and other procedures. On April 29, a large hyphema appeared. In view of the poor light projection and persistence of pain, it was advised to enucleate the globe.

Macroscopic examination revealed a normal cornea. The anterior chamber contained a large hyphema. Both iris and ciliary body were much atrophied. Behind the iris there was an ellipse of compressed, amorphous material resembling lens material and surrounding this some loosely arranged vitreous containing blood. Posterior to this was a completely detached and folded up retina. Behind the retina and in relation to the choroid there was a good deal of albuminous exudate containing tumor cells. At one point the origin of the growth from the external nuclear layer could be made out. The choroid was invaded by cells at one place near the ora serrata. The central part of the vitreous chamber (about 2/3 of the whole) was occupied by the growth. It was a neuroepithelioma containing many rosette formations. Much of the tumor was necrotic but a large part stained well. The optic nerve was intact behind the lamina cribrosa but in front of this there was invasion of neuroepithelioma cells.

This case was accompanied by an excellent picture unequivocally demonstrating rosette formations

In the same year Rasmussen reported a case occurring in a forty eight year old male. The exact nature of this tumor was debatable as there was no photographic evidence and the report was rather nebulous as will be seen in the following summary

A forty eight year old male with a negative past history presented himself in August, 1939 for treatment of keratitis. In October 1940, he was treated again. Treatment had to be reinstituted in November and December of the same year at which time he was hospitalized. Examination at that time revealed a vision of light perception in his right eye and 6/6 in his left eye. There was slight divergence strabismus. The right eye presented ciliary injection with some shagreen of the corneal epithelium and a small macula at 5 o'clock. There were numerous KP's on the corneal epithelium. Posterior synechiae and numerous coarse blood vessels in the iris were noted. Details of the retina could not be determined although the reflex was red. The tension in the right eye was 68 mm. and was normal in the left eye as was the remainder of the examination. The patient was treated with atropine sweating and milk injections. A month after admission an iridectomy was done.

The tension remained unchanged. Pilocarpine was attempted unsuccessfully. The eye quieted down and the pain disappeared. For the following two years he had recurrent episodes of redness and pain in this eye. On November 22, 1944, he was re-admitted after several days of distress. Examination at that time showed no light perception, slight injection, corneal shagreen and slight opacity with dense KP's. The anterior chamber was flat and the iris was atrophic. Enucleation was performed.

Macroscopically, a greyish red soft mass of tissue entirely filled the globe.

Microscopically, a roundish tumor  $16 \times 14$  mm., situated anteriorly in the eyeball, involved all of the structures toward the lens. The tumor was separated from the posterior part of the eyeball by a crescent shaped fissure which was an artefact because all around it there remained tumor tissue corresponding to the site of the retina.

The tumor consisted of large islets of preserved cell masses alternating with great masses of blood and a homogenous coagulate. The tumor cells were preserved chiefly around the numerous vessels. The tumor was built up of cells with round or oval, very strongly stained nuclei, here and there the tumor cells were arranged in not quite typical rosettes. In most places they were very closely packed without structure.

Because of the rosettes this tumor was regarded as a neuroepithelioma but the small number of rosettes and the entire appearance

of the tumor classified it as less mature than the majority of neuroepitheliomas originating from the retina.

O'Day reported the next valid retinoblastoma in an adult in a paper read at the Ophthalmological Society of Australia in Sydney on September 23, 1947.

A twenty nine year old male gave a history of loss of vision and pain in the eyeball after an injury. Examination revealed a visual acuity of hand motion in the temporal field, elevated intra ocular tension and total hyphema. Following a cyclodialysis, the pain and increased tension were relieved. The patient returned one year later after another injury to the same eye with a completely blind and painful globe. On examination at that time, the tension was again elevated, a large globe with a temporal ciliary staphyloma and total hyphema were found. Enucleation was performed.

Opening of the globe revealed a tumor involving the retina, iris, ciliary body and anterior chamber. Tumor cells were seen to be growing along a cyclitic membrane. Microscopic study revealed an infiltrative area in the ciliary body, areas of cells surrounding blood vessels typical of retinoblastoma with numerous mitotic figures. Actively growing areas alternated with necrotic ones. No evidence of extra ocular extension could be found. (There were no pictures or photomicrographs accompanying this report).

In the same year, 1947, Rychener reported the fourth case of a retinoblastoma in an adult as follows:

A thirty three year old female was referred to the author because she noted black spots before the right eye four days previously. Her visual acuity corrected in both eyes was 6/7.5. The right eye was externally normal but ophthalmoscopy disclosed numerous thready and rod pole shaped vitreous opacities which did not cloud the fundus sufficiently to prevent recognition of an unusual cystic lesion below the optic disc which seemed superimposed upon an old chororetinal scar with a superior crescentic boundary of black retinal pigment. The lesion was a three lobed cystic affair, the upper lobe being slightly larger than the disc and about 1 diopter below it covered and invaded by many small vessels giving it a pinkish appearance in contrast to the smooth surfaced grey, translucent appearance of the two much larger lobes which were joined to it below. Peripheral lesions of old disseminated chororetinitis were observed. Transillumination of the mass was normal except for the crescentic line of pigment marking the upper 2/3 of its boundary. Intra ocular pressure was recorded as 13 mm in the right eye and 12 mm in the left eye, Schiotz Potassium iodide was prescribed.

One month later the patient's symptoms were relieved and her visual acuity was recorded as 6/6. She was not seen for the next three years at which time she stated that some dimness of vision

had appeared in the previous two months. Her visual acuity was still recorded as 6/7 5 but the visual field disclosed a large superior temporal defect. The cystic mass had now shrunk into one pedunculated irregular lesion the surface being rough and corrugated. Transillumination was as before and intra ocular tension was normal. On December 23 1943 the vision in the right eye was completely lost returned slightly for a month and then again diminished to light perception. She now exhibited a complete retinal detachment with a crescentic tear up and out at 10 30 o'clock. Transillumination and intra ocular tension were still normal. Enucleation was advised but refused by the patient.

She returned five months later for a refraction of her left eye. The right eye revealed a shallow chamber, a quadrangular pupil and an atrophic iris with newly formed vessels on its surface. The rest of the examination was as before with the exception of an increased intra ocular tension to 50 mm, Schiotz. Enucleation was performed on September 1 1944 and the eye was sent to the Army Institute of Pathology.

Gross examination revealed a firm eye with a dilated pupil. There were firm gelatinous exudates and a pale growth 6 by 7 mm beneath the detached retina. The tumor was situated near the optic disc. The iris and lens were dispatched forward.

Microscopic examination showed a tumor arising in the retina adjacent to the nerve head composed of cells with scant cytoplasm and with round or nearly round nuclei of variable size. Hyperchromatic nuclei and mitotic figures were abundant and in one area there were many large bizarre and multinucleated forms. There was a marked tendency particularly near an area of choroidal invasion toward rosette formation. Here pseudo and incomplete rosettes were seen. Only two or three true Flexner-Wintersteiner rosettes were found in over sixty sections. There was one area of necrosis and around this, clumping of living cells about blood vessels was evident. There were blood vessels and areas of hemorrhage around the tumor. Tumor cells had seeded along the inner and outer retinal surfaces. Adjacent to the tumor the retina had undergone gliosis, fibrosis and calcification. Beneath and peripheral to the tumor there were patchy lymphocytic infiltrations of the choroid with chorioretinal adhesions, secondary pigmentation of the retina and obliterative changes in the retinal vessels.

There were broad peripheral anterior synechiae, a vascular membrane on the anterior surface of the iris and ectropion uveae. The retina was extensively detached. The lamina cribrosa was slightly depressed.

In the discussion of the paper by Rychener, Dr. Georgiana Dvorak-Therobald mentioned another adult retinoblastoma which had been brought to the laboratory of the Illinois Eye and Ear Infirmary.

of the tumor classified it as less mature than the majority of neuroepitheliomas originating from the retina.

O'Day reported the next valid retinoblastoma in an adult in a paper read at the Ophthalmological Society of Australia in Sydney on September 23, 1947.

A twenty nine year old male gave a history of loss of vision and pain in the eyeball after an injury. Examination revealed a visual acuity of hand motion in the temporal field, elevated intraocular tension and total hyphema. Following a cyclodolysis, the pain and increased tension were relieved. The patient returned one year later after another injury to the same eye with a completely blind and painful globe. On examination at that time, the tension was again elevated, a large globe with a temporal choroidal staphyloma and total hyphema were found. Enucleation was performed.

Opening of the globe revealed a tumor involving the retina, iris, ciliary body and anterior chamber. Tumor cells were seen to be growing along a ciliary membrane. Microscopic study revealed an anaplastic area in the ciliary body, areas of cells surrounding blood vessels typical of retinoblastoma with numerous mitotic figures. Actively growing areas alternated with necrotic ones. No evidence of intraocular extension could be found. (There were no pictures or photomicrographs accompanying this report).

In the same year, 1947, Rychener reported the fourth case of a retinoblastoma in an adult as follows:

A thirty three year old female was referred to the author because she noted black spots before the right eye four days previously. Her visual acuity corrected in both eyes was 6/7.5. The right eye was externally normal but ophthalmoscopy disclosed numerous threads and tad pole shaped vitreous opacities which did not cloud the fundus sufficiently to prevent recognition of an unusual cystic lesion below the optic disc which seemed superimposed upon an old chororetinal scar with a superior crescentic boundary of black retinal pigment. The lesion was a three lobed cystic affair, the upper lobe being slightly larger than the disc and about 1 diopter below it, covered and invaded by many small vessels giving it a pinkish appearance in contrast to the smooth surfaced, grey, translucent appearance of the two much larger lobes which were joined to it below. Peripheral lesions of old disseminated chororetinitis were observed. Transillumination of the iris was normal except for the crescentic line of pigment marking the upper 2/3 of its boundary. Intraocular pressure was recorded as 13 mm in the right eye and 12 mm in the left eye. Schlotz Potassium iodide was prescribed.

One month later the patient's symptoms were relieved and her visual acuity was recorded as 6/6. She was not seen for the next three years at which time she stated that some dimness of vision

## DATA CONCERNING THE VASCULAR ORIGIN OF THE DISK EXCAVATION

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As to the development of the disk excavation, the literature records two different views namely the neurogenic and the vasogenic theories. According to the neurogenic theory, the increased intraocular tension which deteriorates the disk by its causing a cavernous degeneration is an essential factor. This fact is proved by the secondary glaucoma in which case it is certain that the excavation is being created by the pressure increase. According to the vasogenic theory, an excavation could appear without any tension increase in consequence of the sclerosis of the blood vessels of the optic nerve due to the insufficient blood supply of the lamina cribrosa. This circumstance is proved by the pseudo glaucoma. The intraocular tension increase in the secondary glaucoma exerts a pressure according to Radnot, Goldmann etc. to the blood vessels of the lamina cribrosa and the final effect is thereby even the vasogenic one.

In our own experiments we have made examinations as regards the vasogenic theory of development of the pseudo glaucoma in connection with 13 cases including 9 women and 4 men patients (Table). The intraocular tension measured by Schiotz's tonometer was a normal one in all of these cases and neither a rise of the eye pressure nor an increase of the chamber angle resistance could have been observed as a result of the provocative tests.

Radiological examinations of these 13 patients have proved a caroti sclerosis on the X Ray photograph of the cranium in 3 of these cases which is according to the earlier literature data (Knapp Thiel) a frequent appearance in case of the disk excavations without glaucoma. In course of our further examinations we have dealt with fixing of the visual field by Flicker Fusion Frequency method. In 8 cases out of 11 we were able to observe a concentrically constricted Flicker Fusion Frequency. This phenomenon could possibly be referred to the statement of Francous according to which the extremely thin art. centr. nervi optici is actually the feeding vessel of the optic nerve. The blood circulation could in this art. centr. n. optici very easily become defective in case of a sclerosis of either the caroti or the art. ophthalmica or the central artery of the optic nerve itself. The development of a state of hypoxia can be observed in cases like that which can be expressed by the concentrically constricted FFF possibly in case of a complete field of vision observed by other methods. In one of the cases we have been observing binasal hemianopia, while in another case an inferior



by Dr. Leon Fordon. This case was never formally reported in the literature, but will be summarized here.

A sixty-six year old female came to her ophthalmologist with the complaint that she could not see to the left with her right eye, following a hit on her head by a window. Examination revealed a large retinal detachment in the lower temporal region of that eye. There was no pain. A reattachment procedure was recommended and refused. Two months later, the detachment became larger and had a peculiar greyish appearance and there was a slight decrease in light transillumination. Enucleation was advised but refused until four months later at which time the eye had become painful. At that time the eye had no light perception, and the tension was 60 mm. Transillumination was negligible.

Microscopic examination showed a white tumor with a 10 mm base on the choroid and a height of 14 mm.

Microscopic section showed a typical neuroepithelioma, composed almost entirely of mature cells arranged in rosettes, most of which were round and many showed no connection with the retina and the base of the tumor invaded the choroid, suggesting that the tumor might be metastatic. Serial section, however, showed origin to be the outer nuclear and the rod and cone layer of the retina. The sides of the tumor were covered with a thick dense vascular connective tissue membrane, which probably encapsulated the tumor except at its origin, until its sudden expansion. This fact suggested the possibility that the tumor may have been present in a quiescent stage for some time. There were no areas of necrosis.

### SUMMARY

The brain metastasis caused the death of the patient. This was the first such specimen found in which a benign melanoma had simultaneously grown.

A case of retinoblastoma and simultaneous benign Schwannian melanoma in a senile patient was presented. The typical cytologic and histologic features and characteristic clinical course with spread to the choroid about the disc seedlings to the iris and eventual brain metastasis made the diagnosis certain.

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hemianopia. Taking no consideration to the X Ray photograph of the skull and to the FFF, the scleral rigidity was below 0 0, 17 (0 0, 08-0 0 13) in 5 cases out of 8 and in 3 cases it was below 0 0 2. In this regard we have to mention the case of two elderly sisters whose value of rigidity was 0 0 08 and the case of a younger patient who was suffering of a one side pseudoglaucoma with a deep excavation and had a completely normal disk on the other side. The scleral rigidity was 0 0, 24 on the sound eye, while on the eye with the excavated disk it was 0 0 13. This means that the congenitally low rigidity of the sclera could create a predisposition to a pseudoglaucomatous excavation.

A rather peculiar phenomenon was the fact that in a certain part of the cases with decreased scleral rigidity we were able to observe smaller oscillations than the normal ones in the oscillogram taken from the upper arms of the patients which is a sign of a hypoplasious blood vessel system. It also occurred that the oscillations were lower on the side of the eye with decreased rigidity than on the other side.

Summarizing all the above mentioned data we are able to state that the disk excavation is a vasogenic process in pseudoglaucoma which develops in consequence of the sclerosis of the optic nerve's own blood vessels. The FFF perimetric narrowing is an introduction of the vasogenic hypoxia. The lower rigidity of the sclera is a predisposing factor.

I take this opportunity to thank the National Council to Combat Blindness Inc. who were kind enough to enable us to accomplish a part of these examinations.

Table

Case No	Sex	Age	Blood pressure	Fluor	X ray	Oscillometry	Rugiditas /R/ Outflow coeff /c/
1	Female	78	180/100	Conc lowered		36	R 008 C 0 24
2		76		Basal hemian			R 01
3		72	190/100	Conc lowered	caroti sclerosis		
4		70	150/100				
5		41	140/80				
6		46	110/70	Normal		401d 221s	Rod 02 Ros 013 Cou 0 25
7		33	100/70			16	R 017 C 0 20
8		42	140/90	Normal			R 008 C 0 24
9		55	120/90	Conc lowered	caroti sclerosis	28	R 017 C 0 24
10	Male	70	130 80				
11		60		Hemianopia inferior			
12		46	120 80	Conc lowered		40	R 008 C 0 24
13		17	100 70				R 017 C 0 22

1 and 2 cases are sisters

hemianopia. Taking no consideration to the X Ray photograph of the skull and to the FFF the scleral rigidity was below 00, 17 (00 08-00 13) in 5 cases out of 8 and in 3 cases it was below 00 2. In this regard we have to mention the case of two elderly sisters whose value of rigidity was 00 08 and the case of a younger patient who was suffering of a one side pseudoglaucoma with a deep excavation and had a completely normal disk on the other side. The scleral rigidity was 00 24 on the sound eye, while on the eye with the excavated disk it was 00, 13. This means that the congenitally low rigidity of the sclera could create a predisposition to a pseudoglaucomatous excavation.

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## A NEW METHOD OF CLINICAL STUDIES FOR OPTIC NERVE HYPEREMIA

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(Director Prof. K. OHASHI)

Pressure on the eyeballs produce functional changes in various organs of the body which are under the control of the autonomic nervous system. This well known phenomenon is called Ashner's phenomenon. Together with changes which occur in the entire body as a result of pressure on the eyeballs, it is expected that changes also occur in the eyeballs themselves.

The accurate measurement of vessel caliber of the ocular fundus is of great importance in the diagnosis and determination of prognosis of diseases of the fundus or general diseases accompanied by changes in the ocular fundus. So far there has been no simple clinical method of accurately describing changes in the ocular fundus when examined ophthalmoscopically, and the observer usually has to depend on his subjectivity. Especially, in ophthalmoscopic examination of diseases of the optic nerve, diagnosis becomes difficult when the change observed is slight.

Numerous reports have already been published on functional changes in various body organs caused by pressure on the eyeballs, however, reports on changes in the retinal vessel caliber caused just after pressure on the eyeballs are seldom seen.

This presentation deals with my attempt to establish a diagnosis method for diseases of the fundus by observing functional changes in the retinal vessel caliber. From these changes the condition of disc hyperemia may be known, and from which an indirect clinical diagnosis of diseases of the optic nerve may be made.

The author's method of measurement is as follows.

The Jikei university method of caliber measurement was further improved by using a Gulstrand's ophthalmoscope and a screw micrometer. The screw micrometer is divided into three parts: the ocular, the gauge and the objective. As shown in fig. 1, the gauge is graduated and by turning the handle the cross in the centre may be moved. After manipulating so that the blood vessel of the subject to be examined is at right angle to the horizontal line at the bottom, the cross is moved to coincide with one wall of the blood vessel. Next, the cross is moved to coincide with the other wall of the vessel. The

reading of the distance which the cross moved is thus taken. Since the micrometer revolves around the optical axis retinal blood vessels running in any direction may be measured.



fig 1 retinal micrometry

#### PRELIMINARY EXPERIMENT

In this experiment the relation between the amount of pressure on the eyeball and the distension ratio of the vessels was studied. By using a Baillart's ophthalmodynamometer pressures of 10, 20, 30, 50 and 100 gm were applied for varying intervals of 1, 2, 3, 5 and 10 min. As a result of this experiment it was determined that the most adequate pressure and duration of time of application were 50 gm and 3 min respectively.

#### PROCEDURE OF THE MEASUREMENT

After sketching the disc and peripapillary retinal vessels with the aid of a hand ophthalmoscope measurements of the vessel caliber of the superior, inferior, temporal and nasal arteries and veins were made at the papillary margin by using the screw micrometer just described. Measurement of the diameter of the disc was also made. Next by means of Baillart's ophthalmodynamometer a pressure of 50 gm was applied directly on the bulbar equator from the outer canthus for 3 min. Directly just after release of pressure, measurements of the vessels just described were again taken. However, the readings on the gauge cannot be taken as the true values of vessel caliber — they must be considered in relation to an object in the retina with a fixed dimension. For this the ratio of the caliber of the retinal vessels to the diameter of the disc was computed according to Lobeck. Also the percentage difference in the caliber of the retinal vessels before and after application of pressure was calculated.

## RESULTS

Aside from the 100 normal eyes used as experimental subjects, the following diseased eyes were also observed 10 papilledema, 5 simple optic atrophy, 5 inflammatory optic atrophy, 5 atypical optic atrophy, 5 retinal optic atrophy, 5 papillitis and 50 retrobulbar optic neuritis. These abnormal eyes showed typical fundus changes and their diagnosis had been confirmed by various other tests.

Micrometric observations were made on the superior nasal artery (ASN), inferior nasal artery (AIN), superior temporal artery (AST), inferior temporal artery (AIT), superior nasal vein (VSN), inferior nasal vein (VIN), superior temporal vein (VST), and inferior temporal vein (VIT). Classification of distension ratio was done as shown in table 1. According to this classification those with lower than

TABLE 1 — retinal vessel calibers and compression ratio of normal eyes

	<i>before compression</i>	<i>after compression</i>	<i>compression ratio</i>
ASN	0.066 ± 0.0009	0.071 ± 0.0012	8.2 ± 0.64
AIN	0.066 ± 0.0014	0.071 ± 0.0015	7.9 ± 0.41
AST	0.077 ± 0.0016	0.086 ± 0.0016	14.8 ± 0.67
AIT	0.075 ± 0.0014	0.086 ± 0.0016	13.8 ± 0.64
VSN	0.086 ± 0.0018	0.097 ± 0.0020	12.2 ± 0.62
VIN	0.086 ± 0.0017	0.092 ± 0.0020	10.3 ± 0.29
VST	0.108 ± 0.0021	0.130 ± 0.0024	20.0 ± 0.90
VIT	0.109 ± 0.0022	0.130 ± 0.0028	18.5 ± 0.58

normal distension ratio, such as -I, -II, -III, have each a difference of five, but those with higher than normal distension ratio such as I, II, III, IV have each a difference of two. Before this classification was made an attempt was made to classify with five each and also two each as the differences for both (—) and (+), however, with these the characteristic curve for each disease could not be obtained. This being the case, it was thought that the mechanism of blood vessel distension differed between the (—) group and the (+) group and so after finding the maximum point of each the present classification was made.

Table 1 shows retinal vessel caliber and distension ratio before and after application of pressure, of 100 normal eyes, excluding those with refraction error. Table 2 shows difference of distension ratio

between arteries and vein of normal eyes Table 3 shows difference of temporal and nasal and table 4 shows difference of upper and lower

TABLE 2—*difference of compression ratio between artery and vein of normal eyes*

	artery	vein	difference
SN	$8.2 \pm 0.64$	$12.2 \pm 0.62$	$3.8 \pm 0.10$
IN	$7.9 \pm 0.47$	$10.3 \pm 0.29$	$2.9 \pm 0.54$
ST	$14.8 \pm 0.67$	$20.0 \pm 0.90$	$5.3 \pm 1.11$
IT	$13.8 \pm 0.64$	$18.5 \pm 0.58$	$4.6 \pm 0.86$

TABLE 3—*difference of compression ratio between nasal and temporal vessel of normal eyes*

	nasal	temporal	difference
AN	$8.2 \pm 0.64$	$14.8 \pm 0.67$	$6.6 \pm 0.92$
AT	$7.9 \pm 0.41$	$13.8 \pm 0.64$	$6.3 \pm 0.76$
NT	$12.2 \pm 0.62$	$20.0 \pm 0.90$	$7.8 \pm 1.09$
NI	$10.3 \pm 0.28$	$18.5 \pm 0.58$	$8.2 \pm 0.65$

TABLE 4—*difference of compression ratio between upper and lower vessels of normal eyes*

	upper	lower	difference
AN	$8.2 \pm 0.64$	$7.9 \pm 0.41$	$0.9 \pm 0.18$
AT	$14.8 \pm 0.67$	$13.8 \pm 0.64$	$0.9 \pm 0.03$
NT	$12.2 \pm 0.62$	$10.3 \pm 0.29$	$2.0 \pm 0.68$
NI	$20.0 \pm 0.90$	$18.5 \pm 0.59$	$1.5 \pm 0.17$

Table 5 shows retinal vessel caliber and distension ratio before and after application of pressure of eyes with optic nerve atrophy. Figs 2, 3, 4, 5 represent this graphically. Table 6 shows papilledema and fig 6 is a graphic representation of same. Table 7 and fig 7 shows early stage of papilledema. Table 8 and fig 8 shows congestion stage and table 9 and fig 9 shows maximum stage. Table 10 and fig 10 shows papillitis and table 11 and fig 11 shows retrobulbar neuritis.



## RESULTS

Aside from the 100 normal eyes used as experimental subjects, the following diseased eyes were also observed 10 papilledema, 5 simple optic atrophy, 5 inflammatory optic atrophy, 5 axial optic atrophy, 5 retinal optic atrophy, 5 papillitis and 50 retrobulbar optic neuritis. These abnormal eyes showed typical fundus changes, and their diagnosis had been confirmed by various other tests.

Micrometric observations were made on the superior nasal artery (ASN), inferior nasal artery (AIN), superior temporal artery (AST), inferior temporal artery (AIT), superior nasal vein (VSN), inferior nasal vein (VIN), superior temporal vein (VST), and inferior temporal vein (VIT). Classification of distension ratio was done as shown in table I. According to this classification those with lower than

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Table 1 shows retinal vessel caliber and distension ratio before and after application of pressure, of 100 normal eyes, excluding those with refraction error. Table 2 shows difference of distension ratio

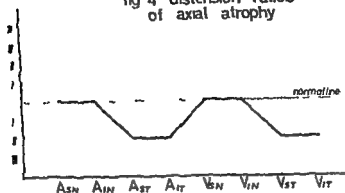
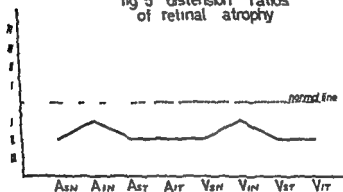
fig 4 distension ratios  
of axial atrophyfig 5 distension ratios  
of retinal atrophy

TABLE E—vessel calibers and compression ratio of choked disc

	calibers mm		ratio %
	before	after	
A <sub>SN</sub>	0.059	0.064	6.8
A <sub>IN</sub>	0.063	0.068	7.9
A <sub>ST</sub>	0.078	0.085	9.0
A <sub>IT</sub>	0.078	0.085	9.0
V <sub>SN</sub>	0.107	0.121	18.6
V <sub>IN</sub>	0.102	0.121	18.6
V <sub>ST</sub>	0.145	0.182	25.5
V <sub>IT</sub>	0.149	0.187	25.5

TABLE 5—*vessel calibers and compression ratio of optic nerve atrophy*

	simple atrophy			inflammatory atrophy			axial atrophy			retinal atrophy		
	bef	aft	ratio	bef	aft	ratio	bef	aft	ratio	bef	aft	ratio
ASN	0.043	0.043	0.0	0.048	0.048	0.0	0.065	0.071	9.2	0.051	0.051	0.0
AIN	0.043	0.043	0.0	0.066	0.067	1.5	0.066	0.071	7.5	0.050	0.051	2.0
AST	0.051	0.052	2.0	0.073	0.074	1.4	0.070	0.074	5.2	0.072	0.075	4.2
AIT	0.052	0.054	3.0	0.073	0.075	2.7	0.083	0.089	7.2	0.064	0.064	3.1
VSN	0.058	0.060	3.5	0.076	0.077	1.3	0.081	0.090	11.2	0.079	0.082	3.7
VIN	0.071	0.074	4.2	0.082	0.084	2.4	0.095	0.105	10.6	0.070	0.074	5.8
VST	0.086	0.091	5.8	0.111	0.114	2.7	0.117	0.131	10.6	0.100	0.109	9.0
VIT	0.083	0.088	6.0	0.101	0.106	4.9	0.116	0.132	12.1	0.100	0.108	8.0

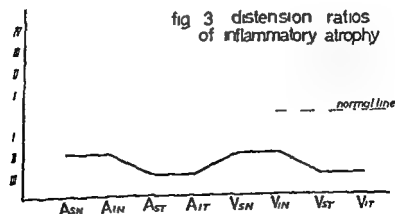
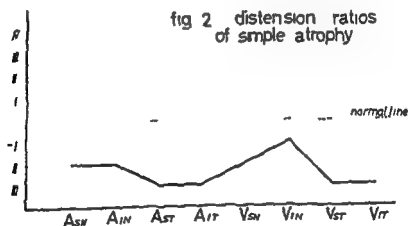
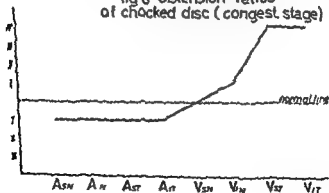


TABLE 8 -- vessel calibers and compression ratio of choked disc (congestion stage)

	calibers in m		ratio %
	before	after	
ASN	0.032	0.034	6.2
AN	0.058	0.061	5.2
AST	0.070	0.077	10.0
AT	0.070	0.076	8.6
VSN	0.067	0.075	12.0
VN	0.096	0.108	12.5
VST	0.128	0.165	29.9
VT	0.139	0.207	30.2

Further studies were made on the hyperemic grade of the disc and distension ratio of the retinal vessels of eyes with retrobulbar neuritis. Those without disc hyperemia or with practically no change in the fundus but with subjective symptoms and central scotoma were referred to as 0 degree; those with slight hyperemia of the disc, but

fig 8 distension ratios  
of choked disc (congest stage)

without other remarkable symptoms as II degree, and those with marked disc hyperemia indistinct disc margin and with irregular reflection in the maculopapillary area as III degree. The curves described by each of these are shown in fig 12, 13, 14.

fig 6 distension ratios  
of choked disc

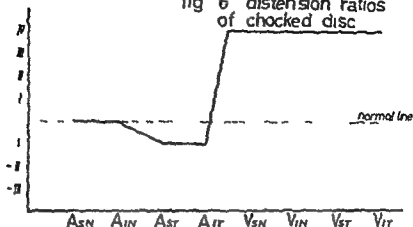
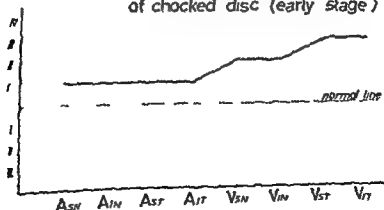


TABLE 7—Vessel calibers and compression ratio of choked disc (early stage)

	calibers m m		ratio of %
	before	after	
ASN	0 080	0 088	10 0
AIN	0 076	0 084	10 5
AST	0 100	0 114	14 0
AIT	0 096	0 107	11 5
VSN	0 096	0 112	16 7
VIN	0 136	0 160	17 6
VST	0 140	0 175	25 0
VIT	0 156	0 196	25 6

fig.7 distension ratios  
of chocked disc (early stage)



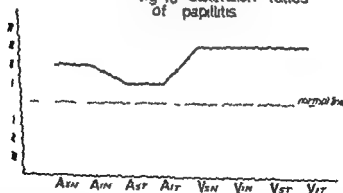
0.5 sec, and inflammatory atrophy in 8-10 sec. Thus indicating that examination of the time of disappearance of redness may also be used as an aid to the early diagnosis of diseases of the disc.

TABLE 10—*vessel calibers and compression ratio of papillitis*

	calibers in m		ratio o/a
	before	after	
Ar <sub>1</sub>	0.903	0.077	11.6
Ar <sub>2</sub>	0.063	0.071	19.7
Ar <sub>3</sub>	0.016	0.093	17.0
Ar <sub>4</sub>	0.082	0.095	15.9
V <sub>1</sub>	0.100	0.118	18.0
V <sub>2</sub>	0.104	0.121	16.4
V <sub>3</sub>	0.151	0.193	26.0
V <sub>4</sub>	0.126	0.157	24.6

With my method it was found that in the normal eye the distension ratio of arteries was approximately 10 per cent and that of the veins above 15 per cent. In simple atrophy and inflammatory atrophy,

Fig. 10 distension ratios of papillitis



the distension ratio of arteries was 0.4 per cent and that of the veins 2.6 per cent. In retinal atrophy, the distension ratio of the arteries was 0.4 per cent and that of the veins 4.9 per cent, indicating that in these abnormal conditions the distension ratio is lowered. In axial atrophy the distension ratios of both arteries and veins were normal.

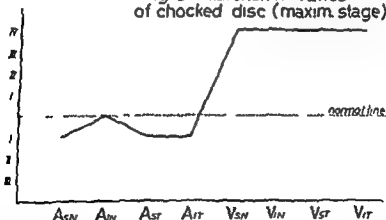
TABLE 9—vessel calibers and compression ratio of choked disc (maximal stage)

	calibers m m		ratio %
	before	after	
ASN	0 061	0 065	6 5
AIN	0 076	0 082	7 9
AST	0 099	0 112	13 1
ART	0 084	0 094	11 9
VSN	0 099	0 119	20 2
VIN	0 107	0 136	21 5
VST	0 141	0 174	30 8
VIT	0 110	0 144	31 0

## DISCUSSION

Foran in 1936 reported that while performing a fundus examination just after applying pressure on the eyeball redness was noted due to dilatation of the retinal vessels. This redness, he stated, took more time to disappear in the eye with inflammatory disc than in the normal eye, whilst in the eye with atrophic disc hardly any redness was noted, or if present only very slight. Thus he termed ophthalmos-angioscopia, and is being applied in the early diagnosis of inflammation

fig 9 distension ratios of choked disc (maxim stage)



or atrophy of the disc. Prof. Ohashi studied the time of disappearance of the redness and reported that the redness disappeared in the normal eye in 9-17 sec., in severe cases of simple atrophy and glaucoma in

I have here described a new functional examination method for observing change in retinal vessels and hope that it will be of aid in the diagnosis and determination of prognosis of fundus disease.

fig 12 distension ratios  
of retrobulbar neuritis  
(hyperemia 0)

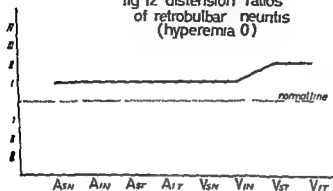


fig 13 distension ratios  
of retrobulbar neuritis  
(hyperemia 1)

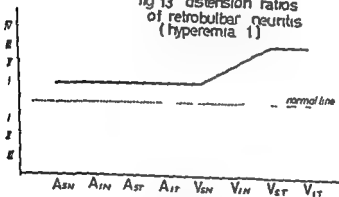
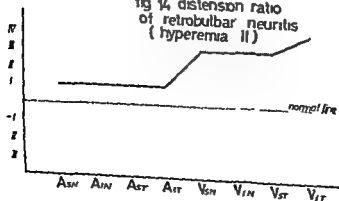


fig 14 distension ratio  
of retrobulbar neuritis  
(hyperemia II)





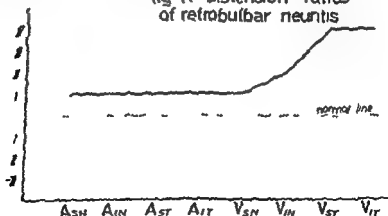
on the nasal side, whereas on the temporal side the distension ratio was markedly lowered

TABLE 11 — vessel calibers and compression ratio of retrobulbar neuritis

	calibers in m		rat o o/o
	before	after	
AS <sub>N</sub>	0 059	0 065	10 2
AT <sub>N</sub>	0 063	0 070	11 1
AS <sub>T</sub>	0 075	0 089	18 7
AT <sub>T</sub>	0 077	0 090	17 0
VS <sub>N</sub>	0 080	0 092	15 0
VT <sub>N</sub>	0 086	0 098	14 0
VS <sub>T</sub>	0 111	0 140	26 0
VT <sub>T</sub>	0 117	0 147	25 8

In papilledema, the distension ratio of the arteries was 7-9 per cent, and nearly normal, whereas that of the veins was 19-26 per cent, and considerably high. In papillitis, both the arteries and veins were considerably distended, especially the veins, but not so remarkable as in papilledema. In retrobulbar neuritis as in papillitis, distension was

fig 11 distension ratios  
of retrobulbar neuritis



observed on both the nasal and temporal sides, however, in the arteries the differences on both sides were of the I degree and only slight, but in the veins, although on the nasal side the difference was of the I-II degree, on the temporal side, the difference was of the III degree

**INTRA CRANIAL PART** It is supplied mainly by a branch of the anterior superior hypophyseal artery from the internal carotid artery. No 'pre chiasmal artery' of Dawson (1948, 1958) was seen. In addition minute collateral branches of variable number from the intra cranial and intra canicular parts of the ophthalmic artery, which mostly run back to ramify on the pia, supply it. The findings of Steele and Blunt (1956) agreed with those of mine. Supply from the anterior cerebral and anterior communicating arteries has also been described by many authors (Wolff 1939, Magitot 1947, Francois et al, 1954 Hughes, 1958 and others)

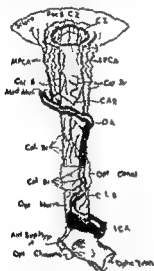


FIG 1 Sources of peripapillary arterial supply to the various parts of the Optic Nerve as seen from above

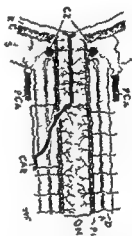


FIG 2 Schematic section of the Optic Nerve and Eyeball showing the pattern of arterial supply to the Intra-orbital and Intra-ocular parts of the nerve

**INTRA CANALICULAR PART** Small collateral branches from the intra canicular and proximal intra-orbital parts of the ophthalmic artery supply this part with a rare contribution by twigs from other sources e.g. central retinal artery or other orbital branches of the ophthalmic artery. These branches reach the nerve through fibrous tissue bands connecting the nerve with the surrounding dura. A rupture of which during head injury may lead to haemorrhages and optic atrophy.

**INTRA ORBITAL PART** It is supplied entirely by the ophthalmic artery.

*Posterior segment* is supplied from the pial vessels which in turn come from the collateral arteries. The collateral arteries usually one

## THE BLOOD SUPPLY OF THE OPTIC NERVE AND ITS CLINICAL SIGNIFICANCE

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Since the time Haller (1754) and Zinn (1755) described an arterial circle in the sclera around the optic nerve, the subject of the blood supply of the optic nerve has been a centre of great controversy. This is because attempts have been made to cover endless variations under single rigid description.

The main controversial issues are

- 1 Origin, branches, distribution and anastomoses of the central retinal artery
- 2 Location, distribution and sources of the axial vascular system in the nerve
- 3 The central artery of the optic nerve
- 4 The blood supply of the lamina cribrosa and the intracranial part of the optic nerve
- 5 Anastomoses between the retinal and ciliary circulations
- 6 A logical interpretation of various clinical conditions in the light of vascular patterns

### ARTERIAL SUPPLY OF THE OPTIC NERVE

For descriptive purposes, the optic nerve is divided into

- (i) Intra cranial part
- (ii) Intra canalicular part — lying in the optic canal
- (iii) Intra orbital part, which can further be subdivided into two parts
  - (i) Posterior segment — lying posterior to (ii)
  - (ii) Anterior segment — in which the central retinal artery runs
- (iv) Intra ocular part, which includes the regions of
  - (i) Lamina cribrosa
  - (ii) Optic disc

**INTRA CRANIAL PART** It is supplied mainly by a branch of the anterior superior hypophyseal artery from the internal carotid artery. No 'pre chiasmal artery' of Dawson (1948, 1958) was seen. In addition minute collateral branches of variable number from the intra cranial and intra canalicular parts of the ophthalmic artery, which, mostly run back to ramify on the pia, supply it. The findings of Sicele and Blunt (1956) agreed with those of mine. Supply from the anterior cerebral and anterior communicating arteries has also been described by many authors (Wolff, 1939; Magitot, 1947; Francois et al 1954; Hughes 1958 and others).

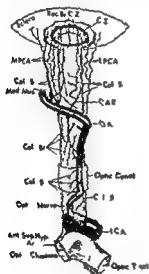


FIG. 1 Sources of peripheral arterial supply to the various parts of the Optic Nerve as seen from above

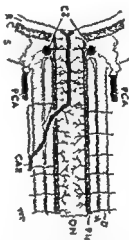


FIG. 2 Schematic section of the Optic Nerve and Eyeball showing the pattern of arterial supply to the Intra-orbital and Intra-ocular parts of the nerve

**INTRA CANALICULAR PART** Small collateral branches from the intra canalicular and proximal intra orbital parts of the ophthalmic artery supply this part with a rare contribution by twigs from other sources e.g., central retinal artery or other orbital branches of the ophthalmic artery. These branches reach the nerve through fibrous tissue bands connecting the nerve with the surrounding dura, a rupture of which during head injury may lead to haemorrhages and optic atrophy.

**INTRA ORBITAL PART** It is supplied entirely by the ophthalmic artery.

*Posterior segment* is supplied from the pial vessels which in turn come from the collateral arteries. The collateral arteries usually one

to three, rarely even more in number, arise usually directly from the ophthalmic artery and less commonly from the central retinal, medial muscular, medial posterior ciliary, posterior ethmoid, supra orbital or other muscular arteries. These are located variably on the optic nerve but rarely on the lateral surface of the nerve.

There is no axial centrifugal vascular system in the intra cranial, intra canalicular and the posterior segment of the intra orbital parts, except for a very rare small recurrent branch from the central retinal artery, which may run back in the centre of the optic nerve in the posterior segment for about 2-3 mm only.

*Anterior segment* contains peripheral centripetal vascular system, as in the other parts, formed by the pial vessels. The pial vessels always come from the central retinal artery, recurrent pial branches of the circle of Zinn and choroidal vessels, and the collateral branches of the ophthalmic artery. In the optic nerve, the distribution of these pial branches from the central retinal artery is reverse of those from the collateral arteries of the ophthalmic, so that it seems one tries to cover up the gaps of the other, while the branches from the circle of Zinn and choroidal vessels are situated all round the nerve.

In addition an axial centrifugal system is seen in this part of the nerve in about 75%, which is always formed by the intra neural branches of the central retinal artery and not by the so called "artery of the optic nerve". The axial system supplies the centre of the nerve to a variable extent in this part of the nerve.

*Anastomoses* All the pial vessels of the optic nerve anastomose freely with one another, particularly in the intra orbital part, before dipping into the nerve and run in its sheath for a variable depth. The anastomoses of the pial branches of the central retinal artery with (a) those from the collateral branches of the ophthalmic artery and (b) the recurrent pial branches from the circle of Zinn and the choroidal arteries are free and prominent. Rarely anastomoses between the axial and peripheral vascular systems are seen.

I want to stress here that the central artery of the optic nerve, as typically described by Behr (1935), Wolff (1939), Francois et al (1954, 1955, 1956), Wybar (1956) and others, was never seen by me. This confirms the findings of Beauvieux and Ristitch (1924), Steele and Blunt (1956) and others. If such an artery at all exists, it is extremely rare, as to be of no significance for all practical purposes. Unfortunately in the recent past a lot of clinical importance has been attached to this artery.

**LAMINA CRIBROSA** It is mostly supplied by branches from the circle of Zinn and also from the choroidal vessels but no branch from the central retinal artery was seen by me in this part. So no anastomoses are seen between the ciliary and the retinal arteries in this region, though such anastomoses at capillary level do exist because of a continuity of the capillary plexus of this region with that of the optic disc anteriorly and the adjoining part of the anterior segment.

of the optic nerve posteriorly. In contrast to this well marked and free anastomoses between the pial branches of the central retinal artery and those of the circle of Zinn and the choroidal vessels are always seen as mentioned above.

**OPTIC DISC** It is supplied by small branches from the central retinal artery and also gets branches from the adjoining choroidal vessels. The capillaries of the disc are continuous with those of the lamina cribrosa posteriorly and the adjoining retina at the disc.

The prominent and free anastomoses of the ophthalmic artery with the surrounding big branches from the external carotid artery e.g. middle meningeal, facial and infra orbital arteries and the arteries of the scalp can usually maintain the blood supply to the optic nerve and the eyeball efficiently in the event of blockage of the internal carotid artery.

#### **VENOUS DRAINAGE**

The blood from the intra ocular and the anterior segment of the intra-orbital part is drained by the central retinal vein. In the posterior segment for a variable distance a prominent tributary of the central retinal vein may be seen lying in the centre of the optic nerve. In addition to these small veins corresponding to the small arteries are seen at places.

#### **VASCULAR DISORDERS OF THE OPTIC NERVE**

I have included many clinical conditions under this category, on direct or indirect suggestive evidence of vascular interference. Future researches and new evidence may relegate some of these to other categories of disorders.

The disorders are classified as follows

#### **I INFLAMMATORY DISORDERS**

- 1 Temporal arteritis
- 2 Periarteritis nodosa
- 3 Thromboangitis obliterans
- 4 Ischaemic optic neuritis
- 5 Fales disease
- 6 Syphilitic optic atrophy

#### **II DEGENERATIVE DISORDERS**

- 1 Cavernous degeneration of the optic nerve
- 2 Cupping of the optic disc
- 3 Glaucoma and pseudoglaucoma
  - (i) Vascular basis of pathological changes in the optic nerve
  - (ii) Vascular basis of the field defects

(iii) Vasogenic basis for glaucoma and pseudoglaucoma

4 Arteriosclerotic optic atrophy

### III THROMBOTIC AND/OR EMBOLIC DISORDERS

1 Occlusion of the central retinal artery

2 Occlusion of the central retinal vein

3 Occlusion of the ophthalmic artery

4 Internal carotid artery insufficiency

### IV VASOMOTOR DISORDERS

Raynaud's disease

### V TRAUMATIC DISORDERS

Optic nerve lesions in head injury

### VI MISCELLANEOUS DISORDERS

1 Papilloedema

2 Optic nerve and retinal haemorrhages in intracranial haemorrhages

3 Post haemorrhagic optic atrophy

4 Compression of the optic nerve

5 Marked oedema of the intra canalicular part of the optic nerve

6 Pulseless disease

7 Altitudinal hemianopias

8 Multiple sclerosis

In such a brief discourse, unfortunately, it is not possible to refer with any justification to any of these disorders. However, it may be pointed out that, in many of these cases, it is not possible to interpret the clinical picture on the basis of the vascular pattern described above. This is because of great discrepancy in our knowledge of aetiology, pathology and pathogenesis of most of the conditions. Perhaps this long list of vascular disorders of the optic nerve may act as a stimulus for more intensive study of all these conditions.

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## ABBREVIATIONS USED

A	= Arachoid
Ant Sup Hyp Art	= Anterior Superior Hypophysial Artery
Br	= Branch
C	= Choroid
CAR	= Central retinal artery
CZ	= Circle of Zinn
Col Br	= Collateral Branch
D	= Dura
ICA	= Internal carotid artery
LPCA	= Lateral posterior ciliary artery
Med Mus	= Medial Muscular
MPCA	= Medial posterior ciliary artery
OA	= Ophthalmic artery
ON	= Optic nerve
PCA	= Posterior ciliary artery
R	= Retina
Rec Br CZ	= Recurrent pial branch of Circle of Zinn
S	= Sclera



## LA TELEVISION RADIOLOGIQUE ET LE CINEMA SIMULTANE EN OPHTALMOLOGIE

par M. NOIX (Paris) et L. SARRAZIN (Nice)

La Television a déjà pénétré parmi les techniques d'exploration de l'oeil et nous rappelons à ce titre les essais de television du fond d'oeil

Mais, en retinoscopie, comme en endoscopie, les résultats, déjà favorables, ne prendront toute leur valeur que lorsqu'il sera possible de réaliser des télétransmissions en couleur. Le noir et blanc ne procurant qu'une reproduction incomplète des contrastes.

Il n'en est pas de même en radiologie où l'on ne recherche que des silhouettes. La Television Radiologique permettra ainsi à l'Ophtalmologiste de développer avec son Collègue Radiologiste des contacts jusqu'alors assez limités.

Si rien jusqu'à présent ne peut remplacer le cliché radiographique classique, il faut reconnaître les avantages que peut apporter à l'investigation ophtalmologique l'utilisation de l'amplificateur de brillance. Cet appareil ramène dans le domaine de la vision mesopique une image radioscopique jusqu'alors confinée dans le cadre restreint de la vision crépusculaire sans possibilité d'appréciation fine des détails.

Mais, en dehors d'une application directe de l'amplificateur à l'examen du squelette orbitaire ou à la recherche d'un corps étranger profond, deux techniques nouvelles viennent étendre les perspectives expérimentales et cliniques relevant de l'ophtalmologie.

Il s'agit d'une part du cinéma radiologique dont le film constitue le document d'ordre dynamique et d'autre part de la Television Radiologique permettant l'observation dans une salle éclairée avec des doses de R<sub>X</sub> très faibles et un coefficient de sécurité exceptionnel pour le malade et l'observateur.

Le cinéma permet de reproduire les différentes phases d'une exploration radiologique, d'où son double intérêt clinique et didactique.

La Television objective en milieu éclairé une image qui appartenait auparavant au domaine de l'obscurité ambiante et pour un seul observateur. Le jumelage Amplificateur de Brilliance chaîne de Television en circuit fermé apporte à l'Ophtalmologiste un procédé d'examen dont nous allons décrire les applications les plus élémentaires, en attendant que l'expérience et le temps en étendent le domaine.

## 1 LES BUTS DU CINÉMA ET DE LA TÉLÉVISION RADIOLOGIQUE EN OPHTALMOLOGIE

Les buts auxquels nous avons pensé sont ceux dans lesquels un élément nouveau au diagnostic et au traitement peut être apporté par la notion du mouvement et est à dire l'exploration du squelette la recherche et l'extraction contrôlée des corps étrangers du globe et de l'orbite l'examen dynamique des voies lacrymales, de la motricité oculaire du nystagmus l'application à la neuro-chirurgie l'angiographie cérébrale et l'étude de la circulation oculaire.

Fig. 1. La télévision radiologique. Une caméra vidicon est jumelée avec un amplificateur de brillance radiologique. L'information après amplification peut être transmise à plusieurs téléviseurs.



(a) Teleradioscopie avec radiographie



(b) Jumelage radio-cinéma teleradioscopie radiographie

1) L'examen du squelette avec l'amplificateur de brillance est une vision radioscopique permettant d'obtenir un centrage plus précis plus judicieux du cliché avec une grande souplesse dans la découverte de l'incidence optimale. L'observateur peut lui-même à tout moment sous le contrôle de la vue mobiliser à la demande la tête du sujet et préciser ainsi l'incidence du trou optique ou de la lèvre sphénoïdale.

2) Le grand coefficient de sécurité permet la localisation exacte et l'extraction des corps étrangers orbitaires ou intra-oculaires surtout lorsqu'il s'agit d'un corps étranger opaque non magnétique.

En effet, en vision crépusculaire le pouvoir séparateur de l'œil dépasse difficilement 30, 4 m/m à la brillance de l'écran radioscopique.

alors qu'il atteint 1 m/m en television radiologique et 5/10 de m/m en examen direct sur amplificateur

(3) Les voies lacrymales pourront être explorées dynamiquement grâce aux différentes phases du transit d'un liquide opaque aux RX. Pendant qu'un aide pratique lentement l'injection, l'observateur mobilisant la tête du malade, pourra découvrir et localiser les sténoses et les diverticules. Une indication thérapeutique précise sera ainsi possible.

(4) La motilité oculaire nous a paru devoir bénéficier de ces techniques et nous vous apportons un exemple des mouvements conjugués des globes. Le déplacement d'index optiques solidaires des cornues par rapport à des repères fixes judicieusement placés permet d'objectiver la motilité normale et pathologique et d'envisager la présence exacte des déviations. Une des applications principales sera l'étude du *nystagmus*, en lumière normale, dans l'obscurité et au cours du sommeil naturel ou artificiel. Le film qui vous sera projeté vous montrera nos premiers essais ainsi que la persistance du *nystagmus* à l'obscurité et son atténuation après l'occlusion des pupilles.

(5) En neuro chirurgie les tumeurs intra ou parasellaires, à retentissement oculaire, devraient bénéficier de l'amplificateur de brillance. La mise en place d'éléments radiotransparents au voisinage de la tumeur, par voie endonasale, doit être grandement facilitée. A tous les instants la direction du trocart porteur des grammes peut être vérifiée sur deux téléviseurs donnant des vues orthogonales de chaque phase du cathétérisme trans ethmoïdo sphénoïdal.

(6) En dehors de ces premières applications d'ordre clinique, la télévision radiologique et le cinéma nous ont permis de reproduire dans un but expérimental et didactique des angiographies cérébrales associées ou non à la ventriculographie. Dans un exemple du regrette Docteur Trotot, il s'agissait d'objectiver un anévrysme de la cérébrale inférieure à retentissement oculaire.

Dans le même ordre d'idée nous portons à l'attention du Physiologiste un essai très imparfait d'opacification des circuits vasculaires d'un oeil de bovidé enclavé se terminant par celle du grand cercle capillaire de l'iris.

Nous espérons ainsi, en démontrant les ressources de l'amplificateur de brillance, provoquer des recherches dans le domaine de la physiologie et de la clinique oculaire.

## II. MATERIEL ET TECHNIQUE D'APPLICATION

Le matériel que nous utilisons pour des premiers essais nous est personnel. Il est constitué par le jumelage d'un amplificateur de brillance et de deux caméras, l'une de cinématographie l'autre de télévision, facilement substituables l'une à l'autre grâce à un système optique d'une grande précision, mais dont la mise au point initiale présente certaines difficultés. Ce système, permet de passer instantanément de l'examen télévisé à la prise du film et par l'adaptation d'un

selecteur radiologique de prendre les clichés radiologiques au temps opportun

Cet ensemble est d'un poids total inférieur à 20 kg. Il est fixé sur une colonne mobile qui en permet le déplacement dans les trois dimensions de l'espace que le malade soit assis ou couché.

Les images téléradioscopiques étant données dans une salle éclairée, aucune adaptation à l'obscurité n'est nécessaire et toutes les manoeuvres chirurgicales peuvent être effectuées avec le maximum de sécurité.

Les clichés radiologiques, pris sous le contrôle de la vue, contiennent les documents statiques indiscutables que le film pourra compléter par des renseignements d'ordre dynamique.

Enfin, signalons que des essais satisfaisants ont été faits sur l'amplificateur de brillance dans le cadre de la reproduction stéréoradioscopique et du film en relief mais que la complexité du matériel laisse ces essais dans le domaine du laboratoire.

### III INTERPRÉTATION DES RÉSULTATS ET AVENIR DE LA MÉTHODE

Nous avons choisi parmi nos documents ceux qui peuvent par une étude comparative montrer la valeur respective du cliché radiologique de l'image de l'amplificateur et de l'image de l'écran de télévision.

Mais le film que nous projetons par ailleurs au cours de ce Congrès montrera par une succession ininterrompue d'images, constituant autant de clichés radiologiques obtenues à la cadence de 16, 24, et même davantage par seconde les différentes phases des examens ci-dessus.

L'avenir seul grâce à l'intérêt que vous voudrez bien accorder à cette méthode permettra de faire un bilan exact des avantages que la Télévision et le cinéma radiologiques auront apporté à l'Ophtalmologie.

Nous souhaitons que cet exposé se traduise par la même étroite collaboration des deux disciplines radiologiques et ophtalmologique que celle qui a permis dans d'autres spécialités d'éclaircir certains points obscurs de la Physiologie viscérale.

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- M Noix 1961 *La télévision radiologique ses problèmes physiques physiologiques et pathologiques* *These de Doctorat es Sciences de l'Université de Paris*  
(16 Mai) Douin Editeur

## OPTIC GLIOMA

ARNOLD TORREST, M D (USA)

Consideration of the problems presented by the glioma of the anterior visual pathways makes clear that there are many more questions than answers. I shall present to you a study of 53 cases which may answer a few more of these questions.

Since gliomatous changes may involve any part of the pathway—the nerve, the chiasm, the tract—the term optic glioma is a useful one because it includes tumor in any of these areas. Among orbital tumors, although optic glioma is uncommon, it is the seventh most frequent pathologic type.<sup>1</sup> In the historical review it is of interest that as recently as 1940 Davis<sup>2</sup> found it necessary to emphasize that intradural orbital tumors may be of two common types. There is today no longer any confusion between these two, namely glioma and meningioma. We shall be concerned only with the glioma. Verhoeff<sup>3</sup> was among the first (1922) to describe the histology of the glioma. He commented further that partial excision was adequate treatment—resulting in apparent clinical cure. Because occasional recurrences have been noted following partial excision, complete excision of the tumor is desirable. A further definition of tumor is given below.

### CLINICAL FEATURES

A study of the literature shows that 90% of patients are less than 20 years of age, the oldest being 60 years. In our series 98% were less than 20 years of age and 80% were less than 10 years of age. The youngest patient showed exophthalmos at birth and the oldest patient was 23 years of age.

The previous medical and family histories are helpful only when a history of von Recklinghausen's disease is present.

In our cases the most common single symptom was exophthalmos. The proptosis was usually downwards, only occasionally upwards or outwards. It averaged 5 millimeters but was as much as 10 millimeters. Tumor in the visual pathway lying only behind the optic foramen does not produce exophthalmos. If the pathway is involved by glioma, the presence of exophthalmos, with rare exceptions, is a necessary and sufficient sign for the diagnosis of glioma in the orbit. Twenty three of 53 patients showed exophthalmos.

The second most common presenting symptom was a visual defect. Since so many patients with optic glioma are very young, poor vision is often overlooked as a symptom and may be difficult to evaluate. Sometimes the visual loss can be measured, but in addition

- M Noix 1959 *La television Radiologique Son Developpement en France*  
Rapport du Congrès International de Munich 1960 *Journal Radiol Electrol*  
Tome 41 No 10 Pages 584-92 et Livre des rapports du Congrès
- I Sarrazin M Noix 1960 *Etude experimentale de la circulation oculaire* (film)  
Congrès International d'Ophthalmologie 'Athènes Livre des Comptes rendus
- M Noix 1961 'La television radiologique ses problèmes physiques physiologiques et pathologiques' *Thèse de Doctorat ès Sciences de l'Université de Paris*  
(16 Mr) Doin Editeur

another hospital was treated by craniotomy when an intracranial mass was identified — then enucleation and excision were performed

Patients with visual defect due to optic glioma but without proptosis carry a much graver prognosis for the reason that the lesion is intracranial. All of these 17 patients received radiation except two who died before it could be carried out. One patient had a subsequent Koenlein operation and is well 18 years later. Two patients are well after 10 and 18 years respectively. Only four have died. Others have been followed less than 4 years.

Patients with strabismus as the most conspicuous symptom present essentially the same problem as those with poor vision. Of these 9 patients one was treated by Koenlein excision and all others have been radiated. Two have died, one is well 10 years later and the others have been followed less than 2 years. Of the patients with increased intracranial pressure 3 of 4 have died but one is well 14 years after radiation. One patient with nystagmus is well 7 years after radiation.

These data represent the relationships of several characteristic symptoms to the site of lesion and subsequent outcome following treatment. How do they determine the management of an individual case?

## DISCUSSION

Any neurologic or x-ray evidence of intracranial involvement by optic glioma immediately places the problem in the hands of the neurosurgeon. Included in the former would be perimetric signs of chiasmal, tract or bilateral nerve involvement. Among the latter would be changes in the sella — V or pear shaped distortion — eroded clinoids, dilated ventricles, involvement of the third ventricle or hypothalamus.

This however leaves unsolved the meaning of dilated optic foramen. One is tempted to assume — *res ipsa loquitur* — that this bony change implies involvement of both orbit and cranial cavity and that exploration of both chambers is mandatory.

However there does not exist a significant study of the tissue derived from both sides or within the canal in patients with optic glioma and radiologically enlarged foramina. There is on the other hand statistical data which has been here presented that excision of the orbital tumor is adequate therapy in many cases. Further pathologic material (Reese & Forrest<sup>23</sup>) has demonstrated that much of the tumor faction in this material is not actual glioma but is reaction of the arachnoid sheath surrounding the nerves or hyperplastic gliosis in the nerve adjacent to the tumor (Figure 1 Sections A and D). The sketch suggests the configuration of some optic gliomas. Either of these changes could result in a dilated foramen but would not constitute tumor on both sides of the canal.

Therefore optic glioma in the orbit without clinical evidence of intracranial disease — even in the presence of the characteristic dilated foramen — should be treated by orbital exploration and excision.



poor fixation and loss of pupillary reflex to light may be noted. When bilateral, blindness is recognizable even in the very young. However, in one patient the vision was 20/20 in each eye.

Strabismus resulted, usually, from loss of vision. Glioma is not an invasive tumor and ocular deviation does not result from involvement of motor nerve or muscle. This contrasts with strabismus which occurs when infiltration results from meningioma or hemangioma. Some patients with optic glioma showed symptoms related to increased intracranial pressure or nystagmus.

Changes in the ocular fundi were common. Of the 23 patients with exophthalmos, all unilateral, 18 showed one normal nerve. On the affected side 15 showed papilledema and 3 showed primary optic atrophy. Two patients had bilateral optic atrophy and in 3 instances there was no comment. In the patients without exophthalmos, unilateral optic atrophy was common, a few patients showed bilateral optic atrophy and a few papilledema on one side and optic atrophy on the other.

Patients with any of these signs and symptoms were studied by X-ray examination of the skull, including measurements of the optic foramina. Those with intracranial disease showed a variety of skull changes involving the sella and the third ventricle. The optic foramina were normal in many of these patients although both optic foramina were dilated in some instances and exophthalmos was rarely present.

Although there is a wide range of normal sizes, a foraminal diameter over 7 millimeters, especially with asymmetry, is strongly suggestive of pathologic dilatation. This is characteristic of optic nerve glioma, although it is also caused by neurofibromatosis, meningioma or retinoblastoma in the orbit.

The exact meaning of the dilated foramen has not been documented in the literature by a study of the soft tissue in the optic canal — nor does any of our cases furnish pathologic material from which precise conclusions can be drawn. We must, therefore, interpret the significance of the dilated foramen in terms of the statistical effect upon the clinical behavior of such tumors.

Twenty three of 53 patients presented with exophthalmos which implied tumor in the orbit. All of these showed a dilated optic foramen. Fifteen of these were treated by Kroenlein orbitotomy alone with excision of the optic nerve mass. Follow up periods range from 16, 11, 10, 10 years and shorter periods. Only in one instance has there been evidence of further disease and this occurred in a patient operated at the age of 6 months — a time when the Kroenlein procedure is technically difficult. In two additional patients, on the basis of a surgeon's report of tumor at the apex, radiation also was given, these patients are well at 4 and 15 years. Another patient was treated by exenteration and is well after a period of 16 years. One patient treated by radiation showed later intracranial recurrence and another following radiation has been well for 11 years. Two patients with evidence of intracranial disease were treated by radiation — one showing continuing disease and one doing well at 6 years. One patient treated at

## SUMMARY — (Contd.)

Patient	X-ray Findings*	Treatment	Follow-up
A. K.	9	Combined	14
C. A.	neg	Kronlein (Tumor at apex)	15
S. C.	5	Radiation	4
A. S.	5 < 6	Kronlein (Tumor at apex)	8
R. H.	8	Radiation	16
M. Mc	4	Kronlein Craniotomy	14
M. M.	—	Ventriculo-pleural shunt	2
F. B.	7	Craniotomy	11
G. E.	—	Biopsy-canthotomy	apathetic drowsy
W. R.	6 5	Exenteration	6
	—	Radiation Craniotomy	
	large	Enucleation V P shunt	
	(v shaped sella)	Radiation	
	large		
	(eroded clinoids,		
VISUAL DEFECT (without proptosis)			
L. B.	11	Craniotomy (subtotal excision)	22
J. B.	5	Radiation	4
J. A.	8	Kronlein	3
I. Br.	6	Craniotomy	9
L. Bo.	(sella gourd shaped)	Radiation	Terminal
D. C.	Ventriculogram	Radiation	10
L. C.	ICT	Radiation	0
R. F.	J-shaped	Craniotomy	0
R. F.	—	Radiation	5
R. G.	NOF	Radiation	18
J. G.	sella enlarged	Craniotomy	Died
W. I.	IEG	Radiation	Died
	indentation		
	floor III v		
	10		
	II		
	(PEG—neg)		
	Ventriculogram		
	Hypothalam c Tumor		
	Large sella		
	J shaped sella		
	Sella distorted		
	OF large		
	PFG		
	vent large		

Skull changes sizes of foramina etc

Care must be taken to maintain proper orientation of the specimen for study by the pathologist. The proximal end of the tumor should be

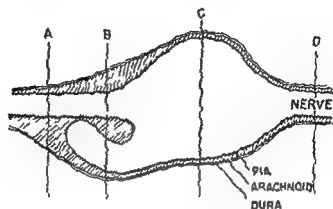


Fig 1 SCHEMA OF OPTIC GLIOMA

studied microscopically and only if retinal glioma is present at this end is craniotomy indicated. If the glioma portion of the tumor has been completely excised there is no need for further treatment.

#### SUMMARY PRESENTING WITH PROPTOSIS

Patient	X ray Findings*	Treatment	Follow up
D L	5	Kronlein	3 yrs 1 & W
L C	6	Kronlein	7
	10		
K D	5	Kronlein	3
	6		
G L	5 x 6	Kronlein	7
	7		
G M	—	Kronlein	1
V N	—	Kronlein	2
D P	—	Craniotomy — neg	1
		Kronlein	
R R	8 x 8	Kronlein	16
	5 x 6		
V S	6 x 7	Kronlein	10
	4 x 5		
R S	7 x 5	Kronlein	1
	4 x 5		
G U	foramen changes	Antrotomy Orbitotomies — neg	13
		Kronlein	
N V	6	Kronlein	14
	8		
L C	5	Kronlein	6
	6 5		

\* Skull changes sizes of foramina etc

## SUMMARY — (Contd.)

Patient	X ray Findings*	Treatment	Follow up
A K	9	Combined	14
C A	neg 5	Kronlein (Tumor at apex)	15
S C	7 5	Radiation Kronlein (Tumor at apex)	4
A S	5 v 6 ■ 4	Radiation Kronlein Craniotomy Ventriculo-pleural shunt Craniotomy	8
R H	—	Biopsy-canthotomy Evacuation	16
M Mc	7	Radiation Craniotomy	14
M M	— 6 5	Enucleation V P shunt Radiation	2
F B	8 N	Kronlein Radiation	11
G E	large —	Radiation	apathetic drowsy
W R	(J shaped sella) large (eroded clinoids,	Radiation	6
VISUAL DEFECT (without proptosis)			
L B	11 5	Craniotomy (subtotal excision) Radiation	22
J B	8 6	Kronlein Craniotomy Radiation	4
J A	(sella gourd shaped) Ventriculogram ICT	Rad at on	3
L Br	J shaped	Radiation Craniotomy	9
I Bo	—	Radiation	Terminal
D C	NOF sella enlarged	Radiation	10
L C	PEG indentation floor III v	Craniotomy Radiation	0
R F	10 5	Craniotomy Radiation	0
R F	(PEG—neg) Ventriculogram Hypothalamic Tumor	Radiation	5
P t	Large sella	Rad at on	18
R G	J shaped sella	Craniotomy	Died
J G	Sella distorted O F large	Radiation	Died
W L	PEG vent larg	Craniotomy (subtotal excision) Radiation	0

Skull changes sizes of foramina, etc.

## SUMMARY—(Contd.)

Patient	X ray Findings*	Treatment	Follow-up
A L	PEG suprasellar tumor	Radiation	4
F N	OF large Ventricles dilated	Craniotomy Torkiben	Died
C P	PEG tumor glioma invading chiasm III ventricle	Radiation	4
J T	3 × 5 7 × 8	Radiation	4

## STRABISMUS

I H	large tumor	Kronlein	1
J H	tumor	Radiation	0
L B	Large N	Radiation	2
	thin dorsum		
I B	J shaped sella	Radiation	1
E G	Ventricles non filling	Radiation	10
I G	5 9 asymmetrical ventricles	Radiation	Died
J I	V shaped sella Large foramina	Ventriculo pleural shunt Radiation	0
S M	PEG suprasellar mass	Radiation	Died

## SYMPTOMS OF INCREASED INTRACRANIAL PRESSURE

J A		Craniotomy	Died
D I	Dilated lateral ventricles	Radiation	14
R R	Fusion clinoids	Craniotomy Radiation	Died
H N	Dorsum destroyed	Craniotomy Torkiben	Died

## NYSTAGMUS

A C	II II	Radiation	7
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## THE CARDONA KERATOPROSTHESIS FIRST CLINICAL EVALUATION

by

HERNANDO CARDONA\*

RAMON CASTROVIEJO†

A GERARD DeVOE‡

Prosthokeratoplasty is the surgical procedure indicated to restore vision when a keratoplasty with either fresh or preserved donor material offers no probabilities of success. In these seemingly hopeless cases a prosthetic corneal implant is the only possible means of achieving any degree of temporary or permanent visual improvement.

### BRIEF HISTORY OF PROSTHOKERATOPLASTY

An artificial cornea was used in one of the first attempts made to improve vision in an eye with corneal opacities. In 1771 Pellier de Quengsy (1) proposed that glass be substituted for opaque corneas. His idea was implemented during the nineteenth century by Nussbaum (2) in 1853, Heusser (3) in 1859, Von Hippel (4) in 1877, and Salzer (5) who used a glass keratoprosthesis in 1898. In 1891 Dimmer (6) used a celluloid plate instead of glass. Further attempts to use artificial corneas were made in 1930 by Verhoeff (7) who used a quartz button. More recently Dorzee (8), Wunsche (9), Kuwabara and associates (10), Gyorffy (11), Franceschetti (12), Vanysek (13), MacPherson and Anderson (14), Stone and associates (15-16), Barraquer (17) and others have used different types of acrylic corneal implants.

The experimental work with keratoprotheses carried out by Stone and his associates at the Ophthalmic Plastics Laboratory of the Massachusetts Eye and Ear Infirmary over the past twelve years deserves to be reviewed at length because they established the basic principles that made possible the definite retention of a plastic implant in a rabbit cornea. In 1953 and again in 1955 Stone reported experimental studies with different models of corneal implants made of annealed methyl methacrylate (15-16). Best results were obtained with

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an implant 12.0 mm in diameter and 1.5 mm thick at the center. It had numerous peripheral holes that Stone hoped would trigger the proliferation of scar tissue through the holes and that in turn this proliferation would lessen the tendency to extrusion. A limbic incision was made, followed by an interlamellar dissection from limbus to limbus. The keratoprosthesis was placed in the interlamellar pocket thus created and the limbic incision closed with interrupted sutures. After a post operative recovery period of variable duration, when cicatrization was sufficiently advanced, a disc 4.0 to 8.0 mm in diameter of the central corneal tissue outside the implant was excised with a trephine. Some of these trephined holes remained patent for a maximum of eight months. In 1958 Stone (18) reported additional data on his experimental work with rabbits. The results proved that the interlamellar implants of his design, with multiple holes to allow for tissue growth, could be maintained indefinitely by a rabbit eye with no tendency to extrusion and that holes trephined in the cornea outside the disc will remain patent for indefinite periods until the natural death of the animal. The longest period of observation reported was 38 months. The center of the plastic disc must be raised 1.0 mm to prevent closure of the trephined area of external cornea over the disc. If this central nubbin is not raised the hole will close.

Once Stone had established the feasibility of indefinite retention of the plastic implant in place by means of patent trephined holes it was necessary to devise a method to make the hole in the corneal layers posterior to the disc and maintain its patency. To this end he designed an instrument with a rotating circular cutting blade that fits behind the cornea in the anterior chamber. The blade was motivated remotely by a series of watch gears. This third stage of the surgical procedure to incorporate an artificial cornea in a rabbit eye, the excision of the corneal layers posterior to the disc, was performed with the instrument just mentioned one or more months after the disc had been placed in the eye and the anterior trephine holes made. According to Stone, if the operation is performed with a minimum of trauma and little bleeding into the anterior chamber, patency is indefinite if the hole does not close within the first ten post operative days.

Five photographs illustrate this most interesting article by Stone with its many ingenious ideas. They show plastic discs in rabbit eyes with holes trephined in the center of the external layers and in the center of the internal layers of corneal tissue. The maximum period of observation until the natural death of the animal with both anterior and posterior trephined openings patent in the same rabbit eye was 34 months for the anterior trephined hole and 29 months for the posterior trephined hole. Neither the ingenious instrument designed by Stone nor the operation is described. The author stresses the use of only the purest plastic material as a prime requisite for a successful outcome. His work in this field is without doubt of great value because he established for the first time the basic principles that must be incorporated in the design of a keratoprosthesis, namely

- (1) An interlamellar skirt or plate to prevent extrusion,
- (2) An anterior central projection in the trephined area to prevent the corneal tissue from proliferating over the face of the implant and
- (3) The use of the purest plastic material available for the manufacture of the keratoprosthesis

Stone also established that the surgical approach must be through a peripheral limbic incision with dissection of an interlamellar pocket as near descemet's membrane as possible

#### CARDONA'S EXPERIMENTAL WORK

After a careful review of the previous work on artificial corneas Cardona concluded that the through and through keratoprosthesis offers the greatest probabilities for obtaining visual improvement but the high percentage of extrusions makes the clinical application of this type of implant impractical. The interlamellar keratoprosthesis gives the best promise for long or indefinite periods of tolerance with no tendency to extrusion. Thus the logical design for a successful keratoprosthesis should combine the through and through optical cylinder for visual purposes and an interlamellar plate to support the cylinder and lower the extrusion rate. The optical cylinder must project anteriorly as advocated by Stone to prevent corneal tissue from growing over the implant but it must also project posteriorly for the same reason. The size of the supporting plate should be reduced to a minimum to lessen surgical trauma but, at the same time to prevent extrusion of the implant sufficient diameter must be preserved. The clinical application of the three stage procedure proposed by Stone although very ingenious and feasible for experimental work with healthy animal corneas would be impractical. A more simple operation should be devised to bring it within the realm of the average ophthalmic surgeon. Since Stone only mentions the use of an instrument with a cutting blade that is introduced inside the eye to make the posterior corneal perforation but fails to describe either the instrument or the surgical maneuver used, it is impossible to judge the merits of either one. It is difficult however to picture the instrument as very effective in the performance in what Stone describes as the cutting of the posterior disc because the manipulation of any instrument no matter how delicate inside an eye likely to require this type of surgery — an eye with no anterior chamber in the process of vitreous prolapse and the eye itself in a state of collapse — would be very near impossible. The operation to be useful clinically must be a simple one preferable a one stage procedure and not a two or three-stage operation as advocated by Stone in the report of his experimental work.

The plastic material used in the manufacture of the keratoprosthesis should naturally be the purest available, prepared and sterilized with the utmost care to insure tolerance by the corneal tissue of the host. Cardona carried out extensive experimental work in rabbit eyes



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at the Nine East Ninety First Street Hospital under the direction of Dr Ramon Castroviejo. Its purpose as already stated was to evaluate in an adequate number of patients the tolerance of human corneal tissue to the implant and the possibility of obtaining either temporary or permanent visual improvement. The patients selected all had badly scarred corneas or eyes in which other types of keratoplasty had failed and the grafts had become either very cloudy or opaque. Their vision was limited to light perception and projection, hand motion or counting fingers at very close range. They were all well within the limits of legal blindness.

Two sizes of keratoprosthesis were used (Fig 2) one with an optical cylinder 1.5 mm in diameter (Fig 2-A) and an anterior projection of 0.65 mm and posterior of from 1.5 mm to 1.8 mm to conform to the greater thickness of the diseased human corneas as compared to that of normal rabbit corneas. The interlamellar plate has a diameter of 3.5 mm. The second prosthesis (Fig 2-B) has an optical cylinder 2.0 mm in diameter. The anterior and posterior projection measurements are the same. In this implant however the interlamellar plate has a diameter of 1.2 mm.

The optical cylinder contains four elements to alternate the refraction index by correcting the spheric, chromatic, lineal and field aberrations. The dioptric power varies from +43 to +63 and is calculated approximately according to the size of the globe and whether or not the eye is aphakic. The positive peripheral and polarization dielectric properties are changed to negative by means of an inductor manufactured by the General Electric Company.

The plastic material is tested by inclusion in rabbit corneas for over six months. It is used only if it does not cause any tissue reactions, an indication that it is neutral and well polymerized. Before surgery the prosthesis including the ocular cylinder and the supporting interlamellar plate is washed in pHisoHex liquid soap and sterilized by immersion in 7ephiran solution 1:750 for 48 hours, followed by exposure to ultraviolet light for thirty minutes.

#### PROSTHOKERATOPLASTY: SURGICAL TECHNIQUES

The patients included in this study were divided into two series according to whether the cornea was avascular or profusely vascularized. **FIRST SERIES**—Avascular corneas. The original Cardona technique as described in the report on his experimental work in normal rabbit corneas was used in 32 eyes with only minor modifications considered desirable to increase operative efficiency because of the pathologic changes in the human eyes. They were affected either with bullous keratopathy secondary to cataract extraction or had undergone several keratoplasties that had resulted in a cloudy or opaque graft.

This procedure (Fig 3) performed as follows will be called Technique No. 1.

testing eighteen prototypes of plastic implants of different shapes and sizes. Interlamellar discs with no anterior or posterior projection were used but the results were poor and the experiments proved that proliferating corneal tissue would cover the disc unless the plate projected beyond the surrounding host cornea. A basic design with a through and through optical cylinder with a supporting interlamellar plate gave the best results. The interlamellar plate supporting the optical cylinder was then reduced in size. Cardona found that the smaller plate was as effective in preventing extrusion as the larger plate that extends over the whole diameter of the cornea with the added advantage of reducing the surgical trauma inherent in its insertion. Non perforated interlamellar plates were easier to make and appeared to perform as well as the perforated ones, so the implants were made with non perforated interlamellar plates. The final kerato prosthesis used in rabbit eyes has an interlamellar supporting plate 3.5 mm in diameter and an optical cylinder 1.5 mm in diameter (Fig. 1). The optical cylinder projected 0.7 mm beyond the inter lamellar plate both anteriorly and posteriorly.

Many acrylic materials were tested before the final selection was made. The plastic chosen contains two polymers, both polymerized by the action of light. It contains neither propionates nor cyanides, toxic substances present in most commercial acrylic plastics to which corneal cells are extremely sensitive.

The one stage surgical procedure selected as the most practical is relatively simple. A corneal incision is made near the limbus and the cornea split to make a central pocket with an external flap of two thirds of the corneal thickness and an internal flap consisting of the remaining one third. After the corneal flaps are made the cornea is perforated with a trephine through both the external and internal flaps of the pocket. The keratoprosthesis is introduced into the pocket until the projections of the cylinder engage the trephined holes to seal the openings. The operation is finished by closing the corneal incision with interrupted sutures.

Cardona's results (19) in eighty healthy rabbit eyes showed that a one stage interlamellar and through and through prosthetic keratoplasty can be successfully performed and the prosthesis well tolerated for a period of up to fifteen months with no tendency to extrusion. This one stage procedure as developed by Cardona is simple enough and sufficiently tested successfully in rabbit eyes to justify a trial in very unfavorable human eyes to ascertain the tolerance of human ocular tissues to the implant and, at the same time, the possibility of obtaining by prosthetic keratoplasty functional improvement in eyes that cannot benefit from other surgical procedures.

#### CLINICAL TRIAL

The clinical study was initiated in November, 1960, in New York at the Institute of Ophthalmology of Columbia Presbyterian Medical Center under the direction of Dr. A. Gerard DeVoe and simultaneously

(Fig 8), the margin of the corneal incision is deepened with a razor blade knife at a 45° angle away from the cornea and a total full thickness graft 0.5 mm greater in diameter than the excised host cornea is sutured to the edge of the cornea in the recipient eye with 7-0 silk sutures in approximately three fourths of its circumference. The graft is not trephined in the center. The Cardona mushroom prosthesis is then inserted so the cylindrical projection enters the perforation already present in the host cornea. The edge of the graft not previously sutured is then closed with additional 7-0 silk sutures and the space between the graft and the recipient cornea with the Cardona mushroom prosthesis in position, is irrigated with saline solution to wash out any accumulated blood. In some eyes the space between the graft and the host cornea forms an artificial pseudochamber.

Another procedure Technique No. 1 consisting of a split cornea with a buried mushroom prosthesis was also developed jointly by Castroviejo and Cardona (Fig 9). It was used as the original intervention in an eye with advanced bullous keratopathy secondary to cataract extraction. It is performed as follows. An incision is made in the cornea near the limbus in half its circumference. The outer two thirds of the external layers of the cornea are dissected with the spatulated dissector over one half the cornea, including the pupillary area. The anterior corneal flap is then deflected and the posterior corneal flap trephined. The Cardona mushroom implant is then placed in position and the incision closed with 7-0 silk sutures. This patient has been under post-operative observation for only a few weeks and the technique has been described in the full knowledge that the report is premature and the results not yet definitive. However we feel that it merits presentation at this time as it may well provide the final answer to the problems of prosthokeratoplasty. Should this prove to be the case its inclusion here will have served to acquaint other ophthalmic surgeons with a new procedure they may wish to investigate further.

In 1953 Thomas (22) reported a buried implant similar in appearance to the one designed by Cardona. The technique used to keep it in place however is different. Thomas used a lamellar graft about 7.0 mm in diameter and 0.5 mm thick to secure the buried prosthesis. He reported the following results. Four of the six implants were retained and it was possible to examine their full depth with the slit lamp. The central area in two eyes was almost clear and appeared as a small dark hole through the posterior layers of the cornea. In the remaining two eyes the central area appeared slightly grey, the opacity being behind the implant.

An evaluation of the results obtained in this series of 32 eyes with avascular corneas shows that in two the cornea became infected. Apparently the infection was triggered in each case by a severe head cold. Although the infection spread very rapidly it remained localized

(1) A Castroviejo microkeratotome (Fig 4) (20) is used to make a curved corneal incision about 9.0 mm long near the limbus. The depth control mechanism is set at 0.5 mm to avoid corneal perforation (Fig 3-A). This maneuver should be monitored by a sufficiently powerful telescope or surgical microscope.

(2) With a spatulated dissector 1.5 mm wide and 10.0 mm long (Fig 5) (21) an interlamellar pocket is made in the corner (Fig 3-B), including the pupillary area and approximately two thirds of the anterior corneal thickness and one third of the posterior.

(3) With a special trephine 1.5 mm in diameter and straight lateral surfaces, the corner is trephined in the center, cutting through the anterior and posterior layers of the pocket (Fig 3-C). If any portion of the edge of the trephined aperture is irregular it should be trimmed with the aid of a jeweler's forceps and fine curved scissors similar to those used in keratoplasties to finish cutting the corneal discs.

(4) The keratoprosthesis, held by a forceps Cardona especially designed for this purpose (a modification of Castroviejo's cross action forceps for cataract extraction) [(Fig 6)], is introduced into the interlamellar corneal pocket and the anterior and posterior cylindrical sections of the implant inserted in the corneal perforations made with the trephine (Fig 3-D).

(5) The incision is closed with 7-0 silk sutures mounted in a Castroviejo Grieshaber needle No. 82-6 mm or another correspondingly fine one. In a few cases 6-0 silk or catgut sutures were used (Fig 3-E).

Local anesthesia was used unless the patient was uncooperative or extremely tense.

In four of the 32 eyes in which this technique was used the corners were found to be thinner than anticipated and they did not lend themselves well to interlamellar dissection so a modified technique was developed jointly by Castroviejo and Cardona. It consists in replacing the external layers of the corner of the recipient eye with a total keratoplasty to support the through and through keratoprosthesis. This procedure will be called Technique No. 2 (Fig 7).

Thirty-two eyes were operated using Techniques Nos. 1 and 2. In five the prosthesis showed a tendency to extrude. The corneal tissue external to the prosthesis in these eyes was excised over the entire surface of the corner and replaced by a total keratoplasty. The graft was trephined over the cylinder of the prosthesis to engage the external projection of the cylinder in the perforation of the trephined graft. Another four eyes showed impending extrusion of the prosthesis and they were reoperated using Technique No. 2. One again showed a tendency to extrusion and was reoperated for the third time. Two of the remaining three were again operated using a total keratoplasty and a buried mushroom implant. This will be called Technique No. 3. In this procedure, developed jointly by Castroviejo and Cardona,

total keratoplasty with prosthokeratoplasty. Preserved corneas were used as donor material. A third operation was necessary in these cases as the prosthesis again showed a tendency to extrude. In the third intervention fresh corneal material was used for the total keratoplasty supporting the prosthesis. In three of the five eyes operated for the third time the keratoprosthesis has been well tolerated for from fourteen to seventeen months (Fig. 16). It has extruded from the remaining two and in each case the corneal aperture left by the extruded prosthesis cicatrized spontaneously by the formation of granulation tissue (Fig. 17). One of these eyes was reoperated a fourth time, using a total keratoplasty of fresh corneal material to support the keratoprosthesis. The implant in this eye has been tolerated for ten months.

Evaluation of the results in the five eyes operated first with the original Cardona procedure (Technique No. 1) followed by a prosthokeratoplasty with a total keratoplasty to prevent extrusion of the implant shows that four eyes finally tolerated the implant after a total of seventeen operations. In one case when the prosthesis extruded for the third time the patient refused further surgery. The present condition of his eye is the same as before surgery with vision limited to light perception and projection.

Technique No. 2 (total keratoplasty with prosthokeratoplasty) was used in the remaining nineteen eyes with profusely vascularized leukomas. Preserved corneal material was used for the graft in four eyes and fresh in the remaining fifteen. The keratoprosthesis has been well tolerated for seven and nine months in two of the four eyes in which preserved corneas were used. The other two required a second operation and fresh corneal material was used for the keratoplasty supporting the implant. These eyes have shown no tendency to extrusion of the prosthesis for five and seven months. One of the other fifteen eyes in which fresh donor material was used developed an infection that terminated in enucleation performed elsewhere and a second was enucleated because of painful almost absolute glaucoma. The keratoprosthesis has been well tolerated in an additional seven eyes although some of them already show signs of corneal erosion that may lead to extrusion. They will probably require another operation. Another eye was reoperated to prevent impending extrusion of the prosthesis but the cornea remaining after dissection of the granulation tissue over the implant was so thin and friable that it could not support the prosthesis and Cardona's original technique (Technique No. 1) was performed in the graft already sutured in the recipient eye. The implant has now been tolerated for over seven months. In three more eyes with impending extrusion of the implant the corneal tissue anterior and posterior to the prosthesis was highly friable. It was not deemed advisable to attempt another prosthokeratoplasty in these eyes. Instead, to save their integrity the entire host cornea including the prosthesis was excised and replaced by a total keratoplasty of fresh donor material. In the remaining two eyes the prosthesis was about to extrude so they were reoperated using Technique No. 2.



in the corner. There was no response to intensive local and systemic treatment. The eyes were saved by excision of the infected corneal tissue, including the implant, which was replaced by a total keratoplasty of fresh donor material. The grafts in these two have become cloudy. There was no functional improvement but in their present condition these eyes are again candidates for a second prosthokaratoplasty.

Another eye was lost because absolute glaucoma developed, necessitating enucleation. A total keratoplasty had already been performed as well as surgery for a secondary glaucoma not controlled by a combination of local and systemic medication. This eye might have fared better if the glaucoma had been under control before the prosthokaratoplasty was performed. Thus tension should be normalized in eyes with increased intraocular pressure refractory to medication before a prosthokaratoplasty is done.

Figures 10, 11 and 12 show the results of prosthokaratoplasties twelve, seventeen and twenty-four months after the operation and Figures 13, 14 and 15 the results obtained with a mushroom implant buried under a total keratoplasty at three, six and seven post operative months.

At the present time the implant is in place in 29 of the 32 eyes in this series. Some of the patients have been under observation for up to 24 months although ten reoperations, using the techniques described, were required to prevent extrusion of the prosthesis. Although the operations were performed in extremely unfavorable eyes, vision improved in eighteen eyes. It was remarkable in some cases, in one eye reaching 20/25 for distance and Jaeger No. 1 for near and in others 20/30 to 20/60.

The most interesting conclusion to be drawn from the results obtained in these eyes with vascular corners is that the prosthesis can be made to remain in position after one, two, or even three operations in a high percentage of cases with varying degrees of corneal cloudiness or opacification, if the integrity of the collagen fibers is fairly good and the corneal thickness normal or only slightly greater than normal.

**SECOND SERIES**—Dense leukomas profusely vascularized. This series included 25 eyes with profusely vascularized dense leukomas resulting from severe burns, sequela of trachoma or severe ocular inflammation. Technique No. 1 (original Cardona procedure) could be used in some of these eyes but in others, because of irregular thickness, the corners did not lend themselves well to interlamellar dissection. In still others the corneas were too soft and friable and they disintegrated upon manipulation with the instruments.

The following techniques were carried out in these 25 eyes. Technique No. 1 was used in six. In five the prosthesis showed a tendency to impending extrusion, only one tolerating the implant. These five eyes were reoperated using Technique No. 2, consisting of a

it is more difficult to use the trephine when the eye is soft. If the perforation is large it is preferable to close the corneal incision and postpone the operation for several weeks or months until the eye is completely cicatrized. If the perforation occurs because the cornea is thinner than was anticipated Technique No. 2 consisting of a total keratoplasty and a prosthokeratoplasty, is substituted for the original Cardona technique.

When the cornea is thinner than anticipated and cannot support the anterior aspect of the prosthesis it may perforate or break during the dissection of the interlamellar pocket. In this case it is advisable to excise the external layers of the cornea to the limbus and proceed with the modified rather than the original Cardona technique, using a full thickness corneal graft to support the prosthesis. A keratome with micrometrically calibrated depth control (Fig. 4) (20) was developed by Castroviejo to minimize the incidence of these two complications. This instrument makes it possible to incise the cornea to the desired depth. If it is more than 0.5 mm thick a flap of external corneal tissue capable of supporting the prosthesis in position can be dissected and the operation is finished using the original Cardona technique. On the other hand, should the cornea perforate when the instrument is set to cut to a depth of 0.5 mm, it is not thick enough to permit the dissection of an adequate external flap. In this case it is preferable to continue the operation with the modified technique using a total keratoplasty to support the implant.

If the eye is soft at the end of the operation because of fluid or vitreous loss and it is not possible to insert the external extension of the prosthesis into the perforation in the external corneal flap, tension may be increased by injecting preserved vitreous or saline solution and air into the vitreous cavity. A 2 cc syringe with a 30 gauge needle is introduced into the eye through the limbus for this purpose. The increased pressure in the vitreous cavity pushes the posterior corneal flap with the prosthesis into position and the external extension of the implant engages the perforation in the anterior corneal flap. Usually the preserved vitreous or saline solution is injected first to normalize the intravitreal pressure. The air is then injected to create the final sudden increase in tension needed to push the corneal flap outward until it contacts the external corneal flap and the optical cylinder on the implant fits into the corneal perforation.

If blood accumulates between the corneal flaps after dissection of the interlamellar pocket it should be washed out with saline solution.

When the cornea of a badly burned eye is trephined it is sometimes possible to visualize intraocular structures such as the lens which were not previously discernible. If the lens is clear it should not be disturbed. If it is opaque it may be removed at the time of the operation with a forceps (Fig. 18) or delivered with a loupe (Fig. 19) through a limbic incision into the posterior corneal flap. Any dense cataractous or capsular remnants or a pseudomembrane behind the trephined cornea

However, the keratoprostheses in these eyes eventually showed a displacement downward with ultimate burial under the corneal graft after spontaneous healing of the external perforation with densely vascularized granulation tissue.

Evaluation of the results obtained in this second series of 25 eyes demonstrates that the surgical techniques used, whether the original Cardona procedure or the modified one consisting of a keratoplasty with prosthokeratoplasty, did not influence the final outcome. However, in these eyes with dense leukoma, profuse vascularization and pronounced structural alterations of the cornea, especially of the collagen fibers, the prosthesis showed a marked tendency to extrude. Numerous operations were required to keep the implant in position to improve these eyes functionally. In some cases, in an attempt to save the eye, the entire host cornea, including the implant, was replaced by a total keratoplasty.

Of the 25 eyes with profusely vascularized corneas in which prosthokeratoplasties were performed, after a period of observation for as long as two years, the implant remains in position in seventeen eyes after a total of 41 operations. Vision improved in five eyes in one patient from light perception and projection to 20/30 for distance and Jaeger No. 2 for near and in four from light perception to counting fingers at two to five feet.

#### POST OPERATIVE CARE

Neosporin ointment is applied at the end of the operation and the operated eye closed with a monocular dressing with no pressure. If the fellow eye is useful it is not bandaged. The patient is ambulatory during his entire period of hospitalization. The operated eye is dressed daily and Neosporin ointment applied. These daily dressings are continued on an outpatient basis after discharge from the hospital in three to seven days. Sutures usually are removed after the third postoperative week. Treatment thereafter is symptomatic. Daily applications of an antibiotic ophthalmic ointment with cortisone are usually continued for several months. The patient is then observed once monthly for possible tendency of the implant to extrude. In cases of impending extrusion the eye should be reoperated, using one of the indicated techniques already described.

During the entire post operative observation period the patient is maintained on a high protein diet with therapeutic doses of vitamins and other supportive measures to improve his general condition.

#### COMPLICATIONS

**Surgical.** At the time of the operation the instrument used to dissect the interlamellar pocket may perforate the section of the cornea forming its posterior aspect. Should this happen, if the perforation is small, the dissection should be continued until the pocket has been completed and the operation finished as originally planned although

tissue around the implant develops a total full thickness keratoplasty, using fresh donor material to support the keratoprosthesis, should be performed (Fig. 23). When the perforation in an eye from which the keratoprosthesis has already extruded shows no tendency to cicatrize spontaneously with granulation tissue the corneal opening should be closed by a partial penetrating keratoplasty (Figs. 24-25) before endophthalmitis develops. Intensive local and systemic antibiotic treatment should be initiated and therapy continued until all danger of intraocular infection has subsided.

In three of the eyes operated a thin membrane formed over the keratoprosthesis several weeks to months after surgery. This was easily removed by scraping the cornea with a razor blade knife. The outer edges of the cornea surrounding the implant were then trimmed slightly with a very fine, sharp pointed scissors to prevent recurrence.

Fairly profuse hemorrhages occurred in two eyes with vascularized corneas at the time of operation. They persisted for some time post operatively in the vitreous and a pseudomembrane of an as yet undetermined nature formed behind the implant. An operation was performed in one of these eyes in an attempt to remove the pseudomembrane but the outcome was not successful. The vitreous in this eye also showed permanent pathologic changes.

There were no cases of luxation of the implant toward the vitreous cavity in this series of prosthokeratoplasties using the different types of corneal prostheses described.

## CONCLUSIONS

It may be concluded from an evaluation of the results obtained in 81 prosthokeratoplasties performed in 57 eyes that a keratoprosthesis implanted in a cornea with fairly good collagen integrity will be well tolerated in a high percentage of cases. Remarkable functional improvement is obtained in some eyes with periods of observation of up to 24 months. When a prosthokeratoplasty is performed in an eye with a densely vascularized cornea such as those seen after severe burns the keratoprosthesis is not well tolerated and extrudes in a high percentage of cases. Attempts have been made in these eyes to keep the implant in position by means of a corneal graft of either fresh or preserved donor material. However the graft supporting the prosthesis often degenerated within a short time. It then vascularized and assumed the characteristics of the host cornea and the implant extruded unless further surgery was performed to prevent it.

The main conclusions to be drawn from this clinical trial are that the original Cardona prosthokeratoplasty or a slightly modified technique offers a good prognosis for prolonged and perhaps even permanent functional improvement in eyes with fairly good integrity of the collagen fibers. On the other hand in severely vascularized corneas the keratoprosthesis whether or not it is surrounded by a total full thickness graft is not well tolerated and often extrudes within a

may be cut using a forceps and Castroviejo synchiotomy scissors introduced through a limbic incision (Fig 20). However, a clear or extractous lens, extractous remnants or a pseudomembrane may be left undisturbed until the eye has completely recovered from the prosthetikeroplasty. Then, in about three months, the indicated procedure should be carried out to remove any intraocular structures that interfere with vision.

**Post operative.** During the immediate and late post operative period the most serious complication encountered is infection of the corneal tissue surrounding the prosthesis (Fig 21). If an infection should develop specimens should be cultured immediately to determine the causative agent and sensitivity tests run to select the most effective antibiotic. Treatment, however, should be initiated at once without waiting for the results of these tests, with applications of a broad spectrum antibiotic or a combination of antibiotic ophthalmic ointments applied alternately. Antibiotics should also be administered systemically and the patient's general condition improved with a high protein diet and therapeutic doses of vitamins. Intravenous injections of typhoid vaccine should be given to boost the patient's defenses. As soon as the results of the sensitivity tests are known the most effective antibiotic should be administered with no further delay. If the corneal infection continues to progress in spite of this intensive treatment and endophthalmitis threatens the eye, the whole cornea should be excised immediately and replaced by a total full thickness graft (Fig 22) to preserve the integrity of the eye. Local and systemic treatment with antibiotics should be continued until all danger of infection has subsided.

This serious complication occurred in three eyes included in this study and the treatment outlined arrested the infection. Vision in these eyes has remained the same as before the initial prosthetikeroplasty. They are now pending reoperation.

*In seriously diseased corneas with dense leukoma and profuse vascularization recurrent ulcers are a frequent complication during the immediate and late post operative recovery period after a prosthetikeroplasty. They also occur in eyes in which total keratoplasties have been performed but no keratoprosthesis inserted. It is possible that these ulcerations are not caused by the keratoprosthesis but result from a number of other factors: precarious nutrition of the cornea, neurotropic disturbances or perhaps they are immunologic responses. In spite of intensive antibiotic therapy the cornea almost always erodes in these instances and the implant extrudes unless another operation is performed. Of course, reoperation offers a very poor prognosis for tolerance of the implant in these cases.*

By far the most frequent complication, which is more often observed in vascularized opacities, is the slow erosion of the corneal tissue surrounding the implant leading to its extrusion in two to sixteen months. As soon as a seemingly progressive erosion of the corneal

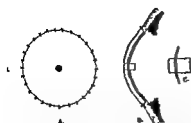


FIG 7 Castroviejo-Cardona total keratoplasty technique with through and through keratoprosthesis

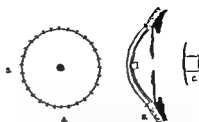


FIG 8 Castroviejo-Cardona total keratoplasty technique with buried Cardona mushroom implant



FIG 9 Castroviejo-Cardona buried mushroom keratoprosthesis technique with split cornea.



FIG 10 Keratoprosthesis in position in a human eye twelve months after the operation.



FIG 11 Keratoprosthesis in position in a human eye seventeen months after the operation.



FIG 12 Keratoprosthesis in position in a human eye 24 months after the operation.

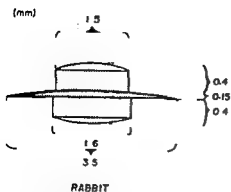


FIG 1 Drawing of Cardona's keratoprosthesis used in rabbit eyes

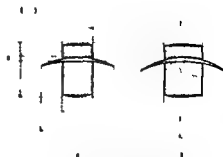


FIG 2 Drawing of Cardona's keratoprosthesis used in human eyes 2 A with an optical cylinder 1.5 mm in diameter and 2 B 2.0 mm in diameter

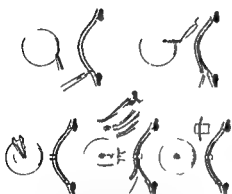


FIG 3 Cardona's prosthokeratoplasty technique with slight modifications as used in human eyes

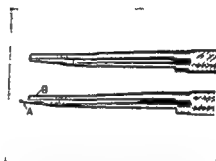


FIG 4 Castroviejo's microkeratotome with depth control mechanism for the cutting blade



FIG 5 Castroviejo's spatulated dissector



FIG 6 Cardona's forceps to hold the keratoprosthesis



FIG 20 Technique for total keratoplasty supporting the keratoprosthesis and excision of dense capsular remnants with Castroviejo synchiotomy scissors



FIG 21 Infection of the corneal tissue surrounding a keratoprosthesis following a severe head cold four months after the operation



FIG 22 Treatment of an infected cornea after prosthokeratoplasty with excision of the entire cornea including the keratoprosthesis which was replaced by a total penetrating graft of fresh donor material

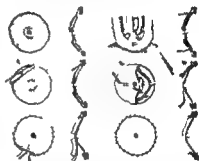


FIG 23 Treatment of corneal erosion around the keratoprosthesis with excision of the external layers of ulcerated corneal tissue and the keratoprosthesis with replacement by a full thickness total keratoplasty and another keratoprosthesis



FIG 24 Small partial penetrating keratoplasty used to close the corneal opening after extrusion of the keratoprosthesis from a human eye



FIG 25 Human eye with a small partial penetrating keratoplasty used to close the corneal perforation after extrusion of the keratoprosthesis





FIG 13 Castroviejo Cardona buried mushroom implant supported by a total keratoplasty in position in a human eye three months after the operation



FIG 14 Castroviejo Cardona buried mushroom keratoprosthesis supported by a total keratoplasty in position in a human eye six months after the operation



FIG 15 Castroviejo Cardona buried mushroom keratoprosthesis supported by a total penetrating keratoplasty in position in a human eye seven months after the operation

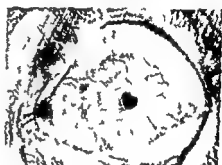


FIG 16 Keratoprosthesis in position in a vascularized human cornea 17 months after the operation



FIG 17 (A) Cardona's keratoprosthesis in position in a human eye with densely vascularized cornea (B) The same eye after extrusion of the keratoprosthesis and spontaneous closure of the corneal opening by granulation tissue



FIG 18 Technique for total keratoplasty supporting the keratoprosthesis and cataract extraction with forceps



FIG 19 Technique for total keratoplasty supporting the keratoprosthesis and cataract extraction with loop

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few weeks or months, sometimes resulting in loss of the eye. In these cases the use of a full thickness corneal graft to support the prosthesis may prevent this complication.

Thus, for patients with an avascular cornea the original Cardona or modified prosthokeratoplasty technique seems to be a valuable addition to the field of corneal surgery. However, eyes with profusely vascularized corneas must be improved structurally before they can be successfully treated by prosthokeratoplasty, performing the corneal graft first and then the prosthokeratoplasty when the eye has recovered from the first operation.

The technique of the full thickness corneal graft to support the keratoprosthesis may be used in some cases as a one stage operation, particularly in patients with limited time for the entire surgical treatment but it is preferable, whenever possible, to improve the cornea structurally and postpone the prosthokeratoplasty until the eye has recovered from the first operation and is in a more favorable condition to undergo a prosthokeratoplasty.

### SUMMARY

The clinical trial of the Cardona prosthokeratoplasty operation is reported as well as some modifications in the techniques required by certain eyes in which the original Cardona operation could not be performed. Other techniques to prevent extrusion of the implant are described. The post operative care and treatment of complications are briefly outlined.

The authors realize that the report of these few cases of artificial corneas will have to stand the test of time but they feel that this branch of corneal surgery has passed from purely animal experimentation to that of clinical application of these new procedures in carefully selected very unfavorable eyes. They present their views in the hope that this report will stimulate the interest of other ophthalmic surgeons in this field and with the combined efforts of many arrive earlier at a more successful and lasting beneficial result from the use of artificial corneas.

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For corneal grafting normal adult animals of known sexes were used as recipients and donors

Corneal heterografts of cat, mouse and bovine tissues varying in thickness and size were transplanted onto rabbits by interlamellar techniques (5) To reduce the host's immune reactions the epithelium was removed from some of the heterografts in others the heterografts were enclosed in specially made intracorneal diffusion chambers described in a previous paper (6)

Full and partial thickness corneal homografts five to seven mm in diameter, were transplanted in rabbits and cats by penetrating, lamellar and interlamellar techniques Some of the interlamellar homografts were enclosed in diffusion chambers

The grafts were removed at different postoperative periods up to a year taking sufficient care not to include any host tissues

A few full thickness and lamellar human grafts were also obtained These grafts were semiopaque and were removed for the purpose of retransplantation The ex of the donors from whom they originally came and that of the patients from whom they were removed were different

For cytological studies, only the transparent animal grafts and the clearest portions of human grafts were cultivated *in vitro* The sex chromatin and chromosome preparations were made from short term cultures

## RESULTS

The results of various experiments will be discussed under the following headings

### 1 THE BEHAVIOUR OF THE CORNEAL CELLS IN TISSUE CULTURE

The cultural characteristics of the cells from the different layers of the cornea viz the epithelium stroma and endothelium varied. In this respect there was also species differences The stromal cells from the corneas of all the mammalian species so far studied could be cultivated readily in the primary short and long term cultures on glass surface Adequate primary outgrowths of the corneal epithelium from all of these species were obtained These epithelial cultures could be maintained satisfactorily for periods up to four weeks But subculturing of these cells by trypsinization was difficult However, we were able to sub-culture the bovine corneal epithelium satisfactorily for three passages and in one instance that of rabbit for two passages With regard to the cultivation of the corneal endothelium, we succeeded in culturing the rabbit's endothelium but so far have obtained inconsistent results with other species With the rabbit endothelium we observed that once the cells started to grow in the

# CYTOLOGICAL STUDIES ON THE CORNEA FOR AN UNDERSTANDING OF THE FATE OF THE CELLULAR ELEMENTS OF HOMO AND HETEROGRAFTS\*

P. K. BASU and P. SARKAR†

This study is a part of a larger investigation on the fate of the cellular elements of corneal grafts, and deals with the karyotypes of man and a few mammalian species as studied in corneal tissues, and the cytology of some of the short term corneal grafts

The use of cytological techniques in our research has been primarily motivated by the idea of using sex chromatin and chromosome complements as biological cell markers for tracing the donor cells following corneal transplantation

Before we could apply these structures to the study of grafts, certain basic investigations had to be performed on normal corneal tissues. As we employed tissue culture techniques exclusively in making cytological preparations, it was important to know whether our *in vitro* methods had any effect on these structures. Furthermore, in view of the possibility of variation of chromosome number in somatic cells (1), it was also necessary to find out whether there was any such inconsistency in the corneal tissues

## METHODS AND MATERIALS

The details of the tissue culture technique and the methods used for making the sex chromatin and chromosome preparations from the tissue culture cells have been described in previous reports (2, 3, 4)

For the preliminary cytological studies various tissues viz., the cornea, sclera, retina, skin, lung and kidney were used from the rabbit, cat, cattle, mouse and man. The preparations of the sex chromatin and chromosomes were made from cells cultivated in the primary short and long term cultures. A cell population which did not undergo more than four passages was termed a short term culture and that which underwent more than four passages a long term culture. The passages were usually made at weekly intervals by trypsinization.

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† This work was supported by a Public Health Grant number 605-7-151.

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## KARYOTYPE OF THE RABBIT

The normal chromosome complement of the rabbit as observed in the corneal stromal cells is shown in figures 1 and 2



FIG 1 The chromosome complement of rabbit (in corneal stromal cell)

The chromosome number of the rabbit is 44 including the X and Y in the male and the two Xs in the female. The karyotype shows paired chromosomes from a typical nucleus of male. It can be seen that the chromosomes fall into distinct groups with respect to total length and arm ratio. The Y chromosome in the male is similar to the two smallest autosomes. The X is a medium sized chromosome with arm ratio of

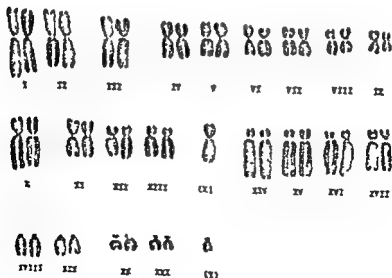


FIG 2 The karyotype of rabbit (male)

primary culture, subsequent short- and long term subculturing by trypsinization was not difficult

In tissue culture, cells from the different layers of the cornea tended to retain their individual morphological appearance, as shown in the primary outgrowth, even in long term cultures. This phenomenon was observed particularly in the epithelial and stromal cells of the cattle and mouse cornea, and in the cells from all the layers of rabbit cornea (4)

## 2 THE EFFECT OF TISSUE CULTURE ON THE SEX CHROMATIN AND CHROMOSOME COMPLEMENTS

Satisfactory sex chromatin preparations were obtained from the different layers of the cornea of man, rabbit and cat. However, due to the variation in number and distribution of heterochromatin bodies in mouse, and particularly in bovine cells, identification of the sex chromatin was difficult in these animals. The percentage of cells with sex chromatin in the stromal cells of the rabbit's cornea was found to be almost constant up to the sixth trypsinized passage, at which time the experiment was discontinued.

The chromosomes were satisfactorily studied in the primary, short and long term cultures of the cells from the different corneal layers of man and animals. The chromosome complements were identical in the primary and short term cultures. In one instance, in a long term culture of the rabbit cornea, the karyotype of the stromal cells was unaltered even up to the 27th passage.

Repeated studies on the primary and short term cultures demonstrated conclusively that cells from both of these cultures were reliable for studying the normal karyotype of an animal. However, it was found that the short term cultures provided better monolayer cell preparations than the primary ones. Therefore, in later experiments we used only short term cultures, and assumed that results obtained from them would be a true indication of the chromosomes of the tissue *in vivo*.

## 3 KARYOTYPES OF THE DIFFERENT MAMMALIAN CORNEAS

In all the mammalian species studied so far, we found that cells from the different layers of cornea had identical chromosome complements. We also observed that the karyotype of the cornea was identical with that of other tissues such as, the sclera, retina, skin, lung and kidney, in the same individual.

A few general characteristics of the chromosome complements of the rabbit, cat, mouse, and cattle as well as that of man are described briefly below. The photomicrographs of the chromosomes were taken with oil immersion lens, and the karyotypes were made from camera lucida drawings.

very great. However, it has been possible to determine the sex of the animals from the chromosomes studied in the corneal tissues grown *in vitro*. The X and Y pair is the second smallest in the complement (number 18). The X is almost metacentric with two equal arms, while the Y is unequally armed. The chromosome number 17 is nucleolar with a conspicuous secondary constriction in one of the arms. There are two pairs, number 15 and 16, of almost telocentric chromosomes. The rest of the chromosomes can be separated into distinct groups according to size and arm ratios as shown in the karyotype (1-3, 4-6, 7-8, 9-10, 11-16). Numbers 1, 2 and 3 are individually identifiable by distinct arm ratios, while the chromosomes in each of the other four groups are similar in size and morphology.

#### KARYOTYPE OF THE CATTLE

The normal chromosome complement of the bull, as observed in the corneal epithelial cells, is shown in figures 5 and 6.



FIG 5 The chromosome complement of cattle (in corneal epithelial cell)

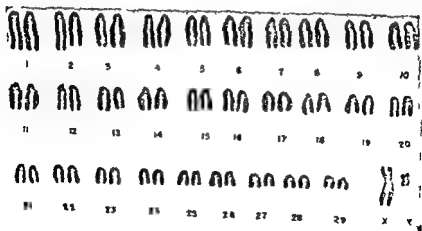


FIG 6 The karyotype of cattle (male)



approximately 1 to 3. The chromosomes numbered 18 and 19 are distinct from the rest in being almost telocentric (4)

#### KARYOTYPE OF THE CAT

The normal chromosome complement of the cat is observed in the corneal stromal cells is shown in figures 3 and 4



FIG 3 The chromosome complement of cat (in corneal stromal cell)

In the somatic cells the cat has 38 chromosomes. The chromosomal sex determining mechanism in the cat is rather subtle in that the morphological difference between the X and Y chromosome is not

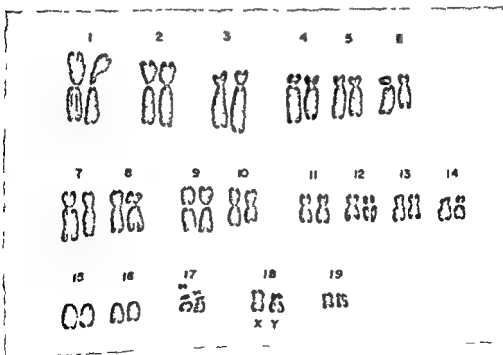


FIG 4 The karyotype of cat (male)

very great. However, it has been possible to determine the sex of the animals from the chromosomes studied in the corneal tissues grown *in vitro*. The X and Y pair is the second smallest in the complement (number 18). The X is almost metacentric with two equal arms, while the Y is unequally armed. The chromosome number 17 is nucleolar with a conspicuous secondary constriction in one of the arms. There are two pairs, number 15 and 16, of almost telocentric chromosomes. The rest of the chromosomes can be separated into distinct groups according to size and arm ratios as shown in the karyotype (1-3, 4-6, 7-8, 9-10, 11-16). Numbers 1, 2, and 3 are individually identifiable by distinct arm ratios, while the chromosomes in each of the other four groups are similar in size and morphology.

#### KARYOTYPE OF THE CATTLE

The normal chromosome complement of the bull, as observed in the corneal epithelial cells, is shown in figures 5 and 6.



FIG. 5. The chromosome complement of cattle (in corneal epithelial cell).

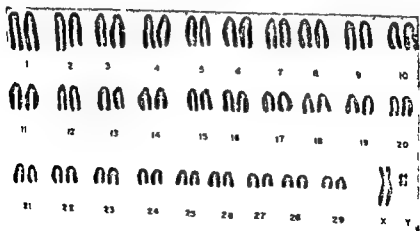


FIG. 6. The karyotype of cattle (male).

approximately 1 to 3. The chromosomes numbered 18 and 19 are distinct from the rest in being almost telocentric (4).

#### KARYOTYPE OF THE CAT

The normal chromosome complement of the cat as observed in the corneal stromal cells is shown in figures 3 and 4.



FIG 3 The chromosome complement of cat (in corneal stromal cell)

In the somatic cells the cat has 38 chromosomes. The chromosomal sex determining mechanism in the cat is rather subtle in that the morphological difference between the X and Y chromosome is not

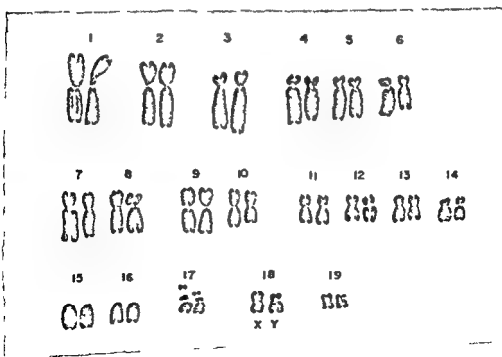


FIG 4 The karyotype of cat (male)

chromosomes we have not attempted to distinguish the sex of the mouse in our chromosome preparations

#### KARYOTYPE OF MAN

The normal karyotype of man, as observed in the *corneal stromal* cells is shown in figures 9 and 10

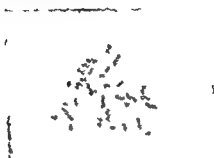


FIG 9 The chromosome complement of man (in corneal stromal cell)

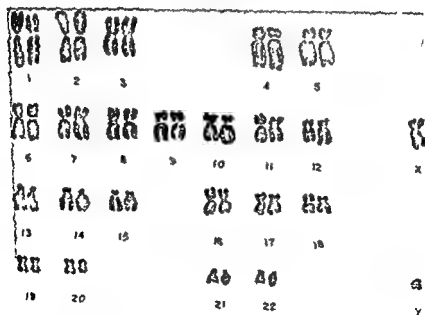


FIG 10 The karyotype of man

In figure 10 the chromosomes have been arranged according to the recommendations of the Denver Convention (7). Our results

A somatic bovine cell contains 60 chromosomes. All the chromosomes except the sex chromosome are almost telocentric. In addition to 29 pairs, or 58 chromosomes, the bull has an X and Y chromosome while the cow has two X's. The sex chromosomes here are very easily distinguishable from the rest of the chromosomes because of their characteristic morphology.

#### KARYOTYPE OF THE MOUSE

The normal chromosome complement of the mouse, as observed in the corneal stromal cells, is shown in figures 7 and 8.



FIG 7 The chromosome complement of mouse (in corneal stromal cell)

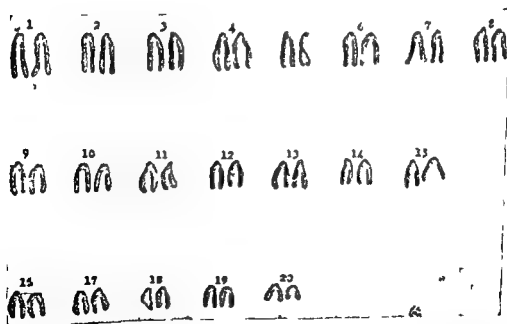


FIG 8 The karyotype of mouse (male)

The chromosome number of the mouse is 10. All the chromosomes are almost telocentric. Because of the difficulty of identifying the sex

12, 13) Table 1 shows the fate of the cellular elements of some of the homografts. It is interesting to note that the original donor cells of the human graft persisted up to 406 days the maximum age of a graft so far studied by us.

TABLE 1 — Fate of the cellular elements of homo- and heterologous corneal grafts

Donor	Host	Type of Graft	Age of Graft	Cell Marker	Identification of original Donor cells
Cat	Cat	Penetrating	306 Days	Sex Chromatin	Positive
Rabbit	Rabbit	Interlamellar	180 Days	Sex Chromatin	Positive
Human	Human	Lamellar	406 Days	Sex Chromatin	Positive
Cat	Rabbit	Interlamellar	43 Days	Karyotype	Positive
Mouse	Rabbit	Interlamellar	52 Days	Karyotype	Positive

Karyological studies on the cells from a few human, and many animal homo- and heterografts are now progressing in our laboratory. We are analysing the number and structure of the chromosomes of the graft at different postoperative periods and comparing them with the normal chromosome complement of the host and the donor.

A cres of cat and mouse full thickness heterografts was transplanted interlamellarly in rabbits. The grafts were removed for cytological studies at intervals of about two weeks. Results obtained from 43 day old cat grafts (6) and 52 day old mouse grafts showed that the original donor cells were viable and cytologically normal (Table 1, Figures 14-15).



FIG. 14 The chromosome complement of a cat corneal heterograft transplanted in a rabbit for 43 days. Metaphase showing 38 chromosomes.



FIG. 15 The chromosome complement of a mouse corneal heterograft transplanted in a rabbit for 52 days. Metaphase showing 40 chromosomes.

show that the human karyotype as studied in the corneal cells is identical with that from other somatic cells (8)

#### 4 THE SEX CHROMATIN AND CHROMOSOME COMPLEMENTS OF CORNEAL GRAFTS

As stated earlier, only clear animal grafts and the most transparent portions of the human grafts were used for culturing, and subsequent cytological analysis. Histological studies made from the remaining portions of the grafts did not reveal any abnormality excepting a few scattered round cells in the human grafts.

The sex chromatin was studied in the cells of a number of homo grafts (human, rabbit and cat) which were transplanted to recipients belonging to the sex opposite to that of the donors. By estimating the percentage of cells containing the sex chromatin in a cell population derived from the grafts, the sex of the tissue was determined (Figs 11,

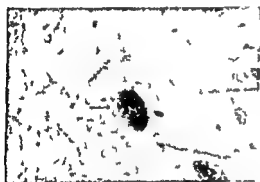


FIG 11 The nucleus of a cell from a cat corneal homograft showing the sex chromatin. The graft came from a female donor and was in a male host for 306 days.



FIG 12 The nucleus of a cell from a rabbit corneal homograft showing no sex chromatin. The graft came from a male donor and was in a female host for 180 days.

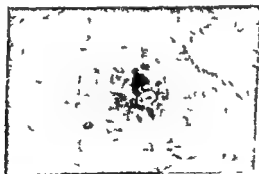


FIG 13 The nucleus of a cell from a human corneal homograft showing no sex chromatin. The graft came from a male donor and was in a female host for 406 days.

graft (which may be called a 'tissue culture *in vivo*') in adapting themselves to a new surrounding would undergo any cytological changes comparable to the behaviour of a cell population *in vitro*.

In our experience different corneal cells *in vitro* appeared to be resistant to any morphological and karyological changes in long term culture. This suggested that the cells of a corneal graft might also show a similar tendency. As mentioned earlier, we have not been able to detect any karyological changes in the few short term heterografts so far studied.

### SUMMARY

- 1 This report deals with the cytology of the normal and grafted corneas of a few mammalian species including man.
- 2 In serial culture cells from the different layers of the cornea tend to maintain their characteristic morphology and cytology.
- 3 The origin of a tissue can be determined by using the sex chromatin and chromosome complements as biological cell markers. These structures are very satisfactorily seen in cells cultivated *in vitro*.
- 4 The karyotypes of the rabbit, cat, cattle, mouse and man as studied in normal corneal cells are described.
- 5 Initial results show that in corneal homo- and heterografts the original donor cells remain viable and cytologically unaltered for a prolonged period (in one instance of a human homograft even for more than a year).

### ACKNOWLEDGMENT

We are grateful to Dr. George A. Thompson who kindly supplied us with the human corneal grafts and to Miss I. Miller and Mr. F. Carré for their technical assistance.

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## DISCUSSION

The present progress in the field of mammalian cytology has been largely possible due to the adaptation of tissue culture techniques for making better cytological preparations. In our studies on the cytology of corneal cells, these techniques have proved to be of great value (2, 4).

In this and in previous studies (3), we have successfully used the sex chromatin as a biological cell marker in the study on the fate of corneal grafts. In the use of sex chromatin, however, certain limitations should be considered. This method is dependent on a very delicate staining procedure as well as on a precise determination in a cell population of the percentage of cells with sex chromatin. It is obvious that in unsuitable preparations, or in the presence of multiple hetero chromatin bodies, as in bovine corneal cells (Fig. 16) the correct

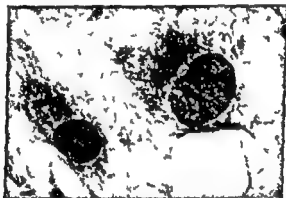


FIG. 16 Nuclei of corneal stromal cells of cattle showing multiple heterochromatin (DNA positive) bodies

assessment of the frequency of the cells showing sex chromatin can be very difficult. The percentage of cells with sex chromatin may also vary over a wide range in different species. Under certain conditions female cells may not even exhibit it, whereas in others, the cells may show duplicate bodies (9).

We thus feel that karyotypic studies give a more precise information about the sex and species of a cell population. Furthermore, these studies enable one to locate any genetic changes expressed in the form of structural alterations of the chromosomes.

With respect to the dispute about the constancy of the chromosome number in somatic cells (1), from our studies we were able to establish that the karyotype of the corneal tissue was identical with that obtained from other somatic tissues in the same species.

It is well known that many kinds of mammalian cells undergo morphological and cytogenetical changes on long term cultivation (10). Therefore, we were also interested to see whether the cells of a

The eye was irrigated with normal saline and the corneal scrapings were inoculated into Czapek or Sabouraud's medium and kept at the laboratory temperature. A portion of the scrapings was stained with lactophenol cotton blue and examined for the presence of hyphae or spores. In the last ten of this series, corneal scrapings were suspended in 5 c.c. of sterile distilled water. Four culture plates were inoculated with one drop of suspension each. For every case all the four plates had the growth of the same fungus. Under identical conditions in the laboratory, a sterile culture plate of Czapek medium was opened



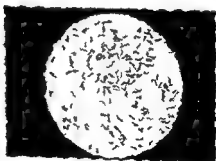
I (Czapek Medium) Culture plate showing the growth of *Actinomyces israeli*



II *Actinomyces israeli*  $\times 400$  granule stained by Lactophenol Cotton blue



III *Fusarium* Culture plate Czapek Medium



IV *Fusarium*  $\times 400$

for ten seconds and closed at the same time. There was no growth in this plate. A drop of fluorescein kept for routine use in the out patient was inoculated into a Czapek medium. In another plate of same medium the nozzle of ointment tube used for patients was touched

## MYCOTIC KERATITIS

E BALAKRISHNAN,

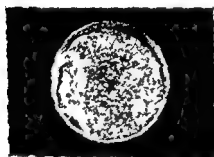
Government Ophthalmic Hospital, Madras, India

Hajano (1910) reported a case of hypopyon ulcer caused by *Aspergillus fumigatus* from Japan. R. H. Elliot (1920) stated that during his term of office as superintendent, Government Ophthalmic Hospital, Madras met with several cases of fungoid infection of the cornea. Makby Kissen and Sine stated that the first case of keratomycosis was recorded in 1933 at the Armed Forces Institute of Pathology. Two more cases were recorded in the next nineteen years and between 1952 to 1956 thirteen more cases were added. Quentin (1937) and Tsutsui (1957) recorded two cases of corneal ulcers caused by *Clostridium Tetani*. Sigtenhorst and Gingrich reported one case of *Nocardia Asteroides*. Anderson B. Roberts and others (1959) have reported four cases of mycotic ulcers. Wendell and Gingrich and Mary E. Pinkerton of Texas (1962) reported a case of corneal ulcer caused by *Actinomycosis bovis*.

In the Government Ophthalmic Hospital, Madras, on an average, three hundred and eighty nine cases of hypopyon ulcers are admitted annually. In the last two years (October 1960 to November 1962) sixty of them were clinically suspected to be of mycotic origin and thirty of them were confirmed by culture. All the patients were adults, twenty of them were males and ten females. All the patients with hypopyon ulcers were working on the farm when the eyes were injured by corn stalk or hay stalk or dust from the soil or chips of wood. After a few hours of injury they had symptoms of watering and photophobia, and sought admission after an interval of about six days on average. None of them had local cortisone or antibiotics and all of them had well established hypopyon ulcers on admission. After examining the lacrimal passage, routine treatment of subconjunctival penicillin, atropine drops and antibiotic ointment was given and the eyes were bandaged. Systemically, sulphur tablets or strepto penicillin were administered for one week. Cases which did not respond were reviewed and the presence of any one of the following signs was taken as suspicious of mycotic ulcer.

- 1 The ulcer being faintly yellow in colour, with beaded border
- 2 Dark brown or black pigments on the floor of the ulcer
- 3 The presence of a hypopyon even when the ulcer is of small size
- 4 Secondary glaucoma

The eye was irrigated with normal saline and the corneal scrapings were inoculated into Czapek or Sabouraud's medium and kept at the laboratory temperature. A portion of the scrapings was stained with lactophenol cotton blue and examined for the presence of hyphae or spores. In the last ten of this series, corneal scrapings were suspended in 5 c.c. of sterile distilled water. Four culture plates were inoculated with one drop of suspension each. For every case all the four plates had the growth of the same fungus. Under identical conditions in the laboratory a sterile culture plate of Czapek medium was opened



I (Czapek Medium) Culture plate showing the growth of *Actinomyces israeli*



II *Actinomyces israeli* / 400 granule stained by Lactophenol Cotton blue



III *Fusarium* Culture plate Czapek Medium



IV *Fusarium*  $\times 400$

for ten seconds and closed at the same time. There was no growth in this plate. A drop of fluorescein kept for routine use in the out patient was inoculated into a Czapek medium. In another plate of same medium the nozzle of ointment tube used for patients was touched

All the plates were incubated at the laboratory temperature and there was no growth in any of these plates. These investigations proved that the cases were not of secondary contaminants.

*An analysis of mycotic infection collected in two years*

TABLE I

Total No. of cases	Males	Females
30	20	10

TABLE II

Hypopyon Ulcers	Granuloma following evisceration	Canaliculitis (lower)
24	4	2

TABLE III

Name of fungi cultured	From corneal ulcers	From granuloma	From canaliculus
<i>Aspergillus fumigatus</i>	13	3	2
Genus <i>Aspergillus</i>		1	
<i>Actinomyces Israelii</i>	2		
<i>Mycelia Sterilans</i>	3		
<i>Blastomyces dermatitis</i>	2		
<i>Helmenthosporium</i>	1		
<i>Fusarium</i>	1		
Unknown fungi	2		

# TREATMENT

Antifungal ophthalmic ointment was not available and so it was not tried. The ulcer was crutered with iodine, mydriatic applied locally and bandaged. Every day the eye was irrigated gently with saline, Nystatin tablets of Squibbs (*Mycostatin* 1 Tab  $\approx$  500,000 units) one tablet i.d.s. for fifteen days was given. Secondary glaucoma was controlled with diamox tablets. Paracentesis was not done.

# COMPLICATIONS

In almost all the cases secondary glaucoma is the commonest complication during treatment. In five cases the ulcer perforated and the prolapsed iris was cauterised by electric cautery. The vascularization of the cornea was not seen in the early stage of the ulcer, but was noted in the late cases. However it was not prominent, and could be detected only by a slit lamp. Complicated cataract could be detected in two of the cases of ulcer due to *Aspergillus fumigatus*.



V *Helmenthosporium*  $\times 400$



VI Corneal Scraping 'Unknown Fungus'  $\times 400$



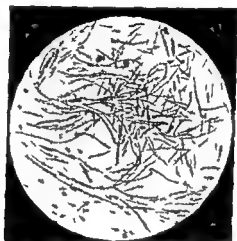
VII *Aspergillus fumigatus*  $\times 600$

# RESULTS

Out of these thirty cases, marked visual improvement was noted only in four of them 6/36 to 6/12. Rest had perception of hand movements due to dense leucomas. In spite of the treatment five ulcers perforated followed by usual complications. In almost all cases of ulcers due to *Aspergillus fumigatus* the pain was relieved and hypopyon was observed within forty-eight hours after administration of mycostatin.

### GRANULOMA FOLLOWING EVISCERATION

Annually about one hundred cases of pinophthalmitis were admitted and eviscerated. During the last two years four of them developed granulomatous mass inside the scleral coat after evisceration, with recurrence of pain and oedema of the lids. In the early stages, the granuloma was soft, later firm and infiltrating into the sclera, when dissected out there was bleeding. Three of these cases were due to *Aspergillus fumigatus* and one was of genus *Aspergillus* and its species could not be identified.



VIII *Mycelia Sterilans*  $\times 400$

### CANALICULITIS

Two cases were of canaliculitis of lower canaliculus due to *Aspergillus fumigatus* and they were relieved after repeated syringing with penicillin solution.

### DISCUSSION

All the hypopyon ulcers occurred in farmers, after minor trauma to the eyes while working in the fields. Pathological fungi cultured from all these cases were proved to survive in the soil (Emmons 1951 and Gohar 1948). So it is inferred that these cases were of primary infection carried from the soil to the cornea due to minor injuries. Sufficient investigations were done to prove that they were not of contaminants from the fluorescein or from the nozzle of the ointment tube commonly used, or from the atmosphere of the laboratory. It is to be noted that in all these cases there was no previous treatment with antibiotics or with corticosteroids.

Due to the absence of specific anti fungal agents, treatment of these cases were not satisfactory. Nystatin and Griseofulvin were the only drugs available in South India. Griseofulvin has no action on the fungi cultured in these cases. Nystatin was therefore administered. Ulcers caused by *Aspergillus fumigatus*, *Blastomyces* and *Helminthosporium* responded well. The exotoxin of *Aspergillus fumigatus*

seems to have been neutralized by Mycostatin administered orally. Blastomyces and Helmenthosporium also seem to secrete exotoxin since they responded well to the systemic administration of Nystatin. Fusarium mentioned in this review was grown on Czapek medium. The identification was based on the appearance of spores which were sickle shaped with pointed ends and with cross septa. Helmenthosporium was grown on potato dextrose medium. Its spores were long roughly cylindrical somewhat attenuated at ends. Actinomyces Israeli was grown on Czapek medium. The growth was very slow, the colonies were snow ball like. The hyphae were about one in in diameter and were branching. They were gram positive and non acid fast. When cultured by Henrich method the granules were very small, yellowish white in colour and were visible to the naked eye. Under the microscope they were polygonal in appearance with a tangle of filaments in the centre. They gradually opened out in periphery as 'clubs' which were acidophilic.

This review brings out the urgent necessity for the search of specific anti fungal agent to reduce the incidence of blindness due to hypopyon ulcers in the agricultural workers.

The fungi reported in this study were cultured and identified by Dr T. K. R. Reddy M.Sc. Ph.D. a mycologist under the guidance of Professor T. S. Sadasivam of Botany Laboratory, Madras University. I should thank Dr T. T. Ramalingam, Superintendent of Government Ophthalmic Hospital and Professor Anantharaman, Head of the Department of Parasitology, Madras Veterinary College for their useful suggestions. I am grateful to Dr (Miss) Marikar M.D., Director of Medical Services of Madras for deputing me to read this paper at the XIX International Congress of Ophthalmology, New Delhi.

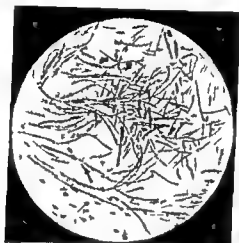
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### GRANULOMA FOLLOWING EVISCERATION

Annually about one hundred cases of panophthalmitis were admitted and eviscerated. During the last two years four of them developed granulomatous mass inside the scleral coat after evisceration, with recurrence of pain and oedema of the lids. In the early stages, the granuloma was soft, later firm and infiltrating into the sclera, when dissected out there was bleeding. Three of these cases were due to *Aspergillus fumigatus* and one was of genus *Aspergillus* and its species could not be identified.



VIII *Mycelia Sterilans*  $\times 400$

### CANALICULITIS

Two cases were of canaliculitis of lower canaliculus due to *Aspergillus fumigatus* and they were relieved after repeated syringing with penicillin solution.

### DISCUSSION

All the hypopyon ulcers occurred in farmers, after minor trauma to the eyes while working in the fields. Pathological fungi cultured from all these cases were proved to survive in the soil (Emmons 1951 and Gohar 1918). So it is inferred that these cases were of primary infection carried from the soil to the cornea due to minor injuries. Sufficient investigations were done to prove that they were not of contaminants from the fluorescein or from the nozzle of the ointment tube commonly used, or from the atmosphere of the laboratory. It is to be noted that in all these cases there was no previous treatment with antibiotics or with corticosteroids.

Due to the absence of specific anti-fungal agents, treatment of these cases were not satisfactory. Nystatin and Griseofulvin were the only drugs available in South India. Griseofulvin has no action on the fungi cultured in these cases. Nystatin was therefore administered. Ulcers caused by *Aspergillus fumigatus*, *Blastosmyces* and *Helmen thosporium* responded well. The exotoxin of *Aspergillus fumigatus*

scrapped and is planted in 9 day embryonated chicken egg for 48 hours  
This can be done in human cornea *in vivo* or in cadaver eyes or even

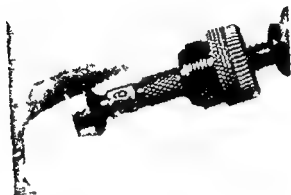


Fig. 1 Solid piston of Castrovejo corneal trephine



Fig. 2 Appearance of Chicken Cornea immediately after it is frozen with solid piston of Castrovejo corneal trephine soaked in CO<sub>2</sub> snow absolute alcohol mixture



Fig. 3 Appearance of Chicken Cornea 2 seconds after application of frozen solid piston of trephine as before



Fig. 4 Normal Cellular Cornea

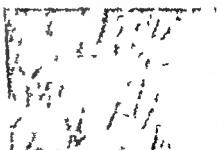


Fig. 5 Acellular Cornea

## ARE THE NON CELLULAR PORTIONS OF THE CORNEA VIABLE?\*

GEMINIANO de OCAMPO, ROMEO B. ESPIRITU,  
SALVADOR R. SALCEDA

*Manila, Philippines*

Frozen or unfrozen glycerin dehydrated corneas used for lamellar keratoplasty preserve their transparency although none of their cells grow in tissue culture (7). When these corneas are embryonated their cells disappear leaving acellular cornea (5). This further shows that their cells were dead. It is claimed that this dehydrated cornea with dead cells is not viable and hence viability of the graft is not necessary for successful lamellar keratoplasty. This is premised on the concept that the non cellular portions of the cornea are non viable. However, this is open to doubt because certainly this dehydrated cornea graft with dead cells does not maintain its transparency like an inert acrylic graft. The question is therefore asked, 'Are the non cellular portions of the cornea viable?' To answer this question is the purpose of this communication.

Almost all previous works on corneal viability have been done on cornea with cells. It seems that by "corneal viability" is meant 'corneal cell viability' which is based solely on culture cell growth. In a previous communication we urged a re-examination of this concept (2). If the cells from the cornea can be removed and the remaining portions studied as to its properties, this question can be enlightened further. This would be a step forward in the study of corneal grafting as well as in other branches of tissue transplantation where the non cellular structures are considered dead (8).

*How an acellular corneal graft is made* To the cornea in vivo and in situ is applied the solid piston of the Castrovieja corneal trephine (Fig. 1) after it has been soaked in carbon dioxide alcohol solution to acquire a temperature of  $-49^{\circ}\text{C}$ . The cornea becomes white (Fig. 2) and in a few minutes resumes its former transparency (Fig. 3). After 48 hours the cornea loses its stromal cells. By scraping the epithelium and endothelium, this cornea becomes completely acellular. This procedure can be repeated with the same result if after instantaneous freezing, the cornea is removed, its epithelium and endothelium

\* Read before the 19th International Congress of Ophthalmology at New Delhi, India Dec. 1962

Supported by a grant from the NSDB and UP

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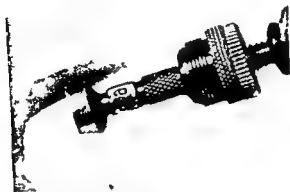


Fig 1 Solid Piston of Castroviejo corneal trephine



Fig 2 Appearance of Chicken Cornea immediately after it is frozen with solid piston of Castroviejo corneal trephine soaked in  $\text{CO}_2$  snow absolute alcohol mixture



Fig 3 Appearance of Chicken Cornea 5 seconds after application of frozen solid piston clear as before



Fig 4 Normal Cellular Cornea

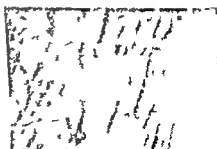


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transparency, slightly clearer than the three King's corneae (7) we have used and equally as good as the cellular lamellar human cornea (3)

In the unfavorable host group (Table 2) after initial transparency they survived with partial or total opacification depending on the extent of unfavorableness of the bed. In two cases where the bed was cauterized with formalin for bleeding they 'took' but although

TABLE 2 — Unfavorable Acellular Lamellar Homotransplants

Age and Size of Graft	Hours after death	Diagnosis	Results
Fresh 7 × 5 mm	5 Hours	Keratitis Dendritic Recurrent OS	Transparency / / / in 24 hours 4 days post-op Dehiscence noted Edema periphery Not fully epithelized Graft opaque a mo after surgery
4 Days 9 / 5 mm	12 Hours	Keratitis Vascularizing Koch OS	Transparency / / / in 24 hours 2 days post-op Intralamellar bleeding Not absorbed w/corneal staining Epithelized in 5 days Good healing Removed on 19th pod for histology
40 Days 9 5 mm	15 Hours	Keratopathy Bullous Aphakia OS	Transparency / / / in 24 hours Clearing up of edema in bed Epithelized in 7 days Good healing Slight edema after 2 mos Partially opaque in 6 mos Minimal deep BV
3 5 Mos 8 5 mm	5 Hours	Corneal Ulcer Torpid OS	Transparency / / / in 24 hours Epithelized in 7 days Edema of graft on 6th day Sutures removed on 14th day Graft detached and opaque the following day
7 5 Mos 9 5 mm	2 Hours	Leucoma Extensive Vascularized (Acid burns) OS	Transparency / / / in 24 hours Good healing Epithelized in 6 days Increase BV in bed Graft hazy on 17th day Under observation.

they survived morphologically for some time they gradually disintegrated like heterografts (Table 3) Whereas the cellular or acellular

in isolated cornea. The embryonation conveniently removes the dead stroma cells. It is by this means that we could obtain from the Philippine General Hospital Cornea Bank all the human acellular corneas that we have used in these clinical and experimental studies.

*Clinical properties of acellular cornea.* Human acellular corneal homograft. We have used so far 24 human acellular corneas for lamellar grafting in various conditions of the host cornea. These may be divided into those favorable without or very minimal vascularization for usual keratoplasty and those unfavorable with extensive leucoma, mostly adherent and vascularized or with active inflammation and/or infection for therapeutic, tectonic and cosmetic keratoplasty. The graft used varied from those freshly taken from the cadaver to those stored in 95% glycerin for variable periods to 1, long as eight months. These grafts have been followed from one month to almost a year now. On the whole, in favorable host beds (Table 1), they survive with full

TABLE 1 — *Favorable Acellular Lamellar Homotransplants*

Age and Size of Graft	Hours after death	Diagnosis	Results
Fresh 9 × 5 mm	7 Hours	Keratitis Interstitial OS	Transparency / / / / in 24 hours. Maintained. Clearing up of edema in bed. Minimal peripheral BV.
10 Days 7 × 5 mm	5 Hours	Pterygium Extensive OD	Transparency + / in 24 hours. Maintained. Epithelialized in 5 days. Good healing. Minimal BV from side of pterygium.
21 Days 9 × 5 mm	10 Hours	Keratitis Superficial Recurrent Viral OS	Transparency / / / / in 24 hours. Maintained. Epithelialized in 6 days. Good healing. Pathology arrested. No vascularization. Granulation T.
25 Days 9 × 5 mm	3 Hours	Keratitis Disciform OS (1 Mo old)	Transparency / / in 24 hours. Maintained. Epithelialized in 6 days. Clearing up of edema in bed. Good healing. Minimal peripheral BV.
11 Mos 9 × 5 mm (Peritom) Partial)	5 Hours	Pterygium Extensive OD	Transparency / / / / in 24 hours. Still clear up to present — 1 Mo after. Epithelialized in 8 days. Good healing under observation.

TABLE 4—Results of Acellular Heterotransplants

Kind Size and Type of Graft	Diagnosis	Results
Fowl Ant Lamellar 7 mm Cosmetic	Leucoma Extensive Vascularized OD	Transparency / / / / in 24 hours Maintained up to 7th day Opaque in 25 days Gradually disintegrated and on 40th day only $\frac{1}{2}$ of Graft left
Fowl Ant Lamellar 7 mm Cosmetic	Leucoma Extensive Vascularized OD	Transparency / / / / in 24 hours Maintained up to 5th day Com- pletely opaque in 50th day Disintegrated and gone 2 $\frac{1}{2}$ months after
Fowl Ant Lamellar 8 mm Cosmetic	Leucoma Extensive Vascularized OD	Transparency / / / in 24 hours Maintained up to 8th day Opaque in 45 days and gone on the 57th day
Fowl Penetrating 6 mm	Leucoma Extensive Vascularized OD	Transparency / / / / in 24 hours Persistent Posterior Edema Completely opaque on 14th day Gradual thinning and anterior bulge 48th day very thin Repeat kerato- plasty

the Warburg apparatus for oxygen consumption. The results are tabulated as follows. (5)

Specimens	Oxygen consumption Co <sub>2</sub>	Results of Langham
Whole Cornea Fresh (Chicken)	0.674 ml/hr/mg	0.864 ml/hr/mg
Cornea w/out epithelium and endothelium Fresh	0.371 ml/hr/mg	0.230 ml/hr/mg
Stored whole cornea for 2 days in liquid paraffin	0.273 ml/hr/mg	
Acellular Cornea Fresh	0.214 ml/hr/mg	



heterografts (4) disintegrated after turning completely opaque these homografts remained slightly transparent until they disintegrated In one case where this acellular human cornea was used for penetrating therapeutic grafting, it survived morphologically but became opaque

Acellular chicken corneas were used in human eyes in four very unfavorable cases (Table 4) for cosmetic and tectonic cases The concept is that they would be less or not at all antigenic because it is

TABLE 3—Initially clear Acellular Lamellar Homografts that became partially opaque and disintegrated

L M	Leucoma Extensive Vascularized OS (Post keratoplasty opacity)	Anterior Lamellar 9 x 5 mm OS Formalin 10% cautery of corneal bed 21 Days stored	Transparency / / / in 24 hours Epithe- lized in 6 days Poor healing No Vascularization A mo after slight haziness, Then gradual disinte- gration from peri- phery Gone in 2 Mos
D A	Leucoma Extensive Vascularized OS (Post keratoplasty opacity)	Anterior Lamellar 9 x 5 mm OS Formalin cautery 10% of corneal bed 10 Days stored	Transparency / / / in 24 hours Epithe- lized in 6 days Delayed healing, No vascularization of graft Edema periphery a month after and gradu- ally disintegrated Gone in a month's time

believed that the corneal antigens come from the cells Although they survived morphologically for about two and a half months which was longer than the cellular chicken heterografts, they eventually disintegrated If the rejection were solely allergic in nature, this in a way showed that the corneal antigens do not come entirely from the corneal cells It was observed that acellular homograft were less invaded by host blood vessels than the cellular graft

All these clinical characteristics of a cellular graft may be interpreted as those of biological survival or viability

*Biochemical properties—Oxygen consumption* Using whole fresh cellular cornea as control, acellular chicken corneas were tested by

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Acellular Cornea Fresh	0.214 ml/hr/mg	

These findings show that acellular cornea consumes some oxygen under room temperature in NSS. It therefore respire although to a lesser extent than cellular cornea.

*Physiological Properties — Hydration and Dehydration Experiments*  
These follow the technique and procedure of Harris experiments on hydration of human cornea. All the corneal specimens were obtained from cadaver's eyes without enucleation. For control and comparison we used acrylic plastic contact lens, gelfilm and formalinized cornea as well as fresh and stored cellular corneas. Essentially the experiments consisted of weighing the specimens initially, after 2 hours in NSS at  $-4^{\circ}\text{C}$  and then after 3 hours in NSS at  $+37^{\circ}\text{C}$ . The results are shown in Table 5.

It will be noted that

- 1 Acrylic plastic contact lens did not show any change of weight
- 2 Gelfilm increased in weight at  $-4^{\circ}\text{C}$  and more in  $+37^{\circ}\text{C}$
- 3 Cellular cornea weighed a little more at  $-4^{\circ}\text{C}$  but much less at  $+37^{\circ}\text{C}$
- 4 Acellular cornea weighed more at  $+4^{\circ}\text{C}$  but like the cellular cornea it could dehydrate and weighed less at  $+37^{\circ}\text{C}$
- 5 When formalinized however, this property of hydration at  $-4^{\circ}\text{C}$  and dehydration at  $+37^{\circ}\text{C}$  decreased considerably but it was not completely lost.

TABLE 5 — Summary of Hydration Experiments on human corneas

Specimens	Initial Wgt	Wgt after 2 Hrs in NSS at $+4^{\circ}\text{C}$	Wgt after 3 Hrs in NSS at $+37^{\circ}\text{C}$
Acrylic Plastic	20.9 mgs	20.9 mgs	20.9 mgs
Gelfilm	12.8 mgs	28.6 mgs	31.1 mgs
Cornea Cellular Fresh	127.5 mgs	128.8 mgs	120.1 mgs
Cornea Cellular Stored	136.2 mgs	137.8 mgs	109.3 mgs
Cornea, Acellular Fresh	129.2 mgs	151.3 mgs	131.8 mgs
Cornea Acellular Stored	105.2 mgs	127.0 mgs	101.9 mgs
Cornea Acellular Formalinized	91.3 mgs	85.3 mgs	87.1 mgs

Adapted after Harris Experiments

These experiments show that acellular cornea has the property of hydration and dehydration.

### Biological properties - Incorporation Studies

#### PROCEDURE

1 Left cornea of chicken frozen with  $\text{CO}_2$  snow absolute alcohol mixture

- 2 250 microcuries of S35 as sodium sulfate injected subconjunctivally to each eye 48 hours later
- 3 Both corneas were removed 24 hours after injections
- 4 Unattached S35 removed by washing in several changes of water then fixed in 10% formalin
- 5 Radio activity determined quantitatively with scintillation detector and Geiger counter

#### RESULTS:

##### A Scintillation Counter

Background	83 counts/min
Count rate of S35 (324 micro curies)	42 counts/min
Count rate of acellular cornea	Activity not high enough
Count rate of cellular cornea	To be recorded by the detector. Counts almost the same as background

##### B Geiger Counter

Background	8.5 counts/min
Count rate of S35 (324 micro curies)	27 counts/min
Count rate of acellular	11 counts/min
Count rate of cellular	0.8 counts/min

*Remarks* Acellular cornea also incorporates the radio isotopes. In fact it even had a little higher concentration than the cellular cornea.

#### AUTORADIOGRAPHY

- 1 Left cornea of chicken frozen with CO<sub>2</sub> snow absolute alcohol mixture
- 2 250 microcuries of S35 as sodium sulfate injected subconjunctivally to each eye 48 hours later
- 3 Both corneas removed 24 hours after injections
- 4 Unattached S35 removed by washing corneas, fixed in 10% formalin and prepared for histopathology
- 5 Sections placed in glass slides and covered with radiographic stripping film (Kodak AR 10)
- 6 Preparations placed in light tight boxes
- 7 Film together with slide developed at intervals of 2 to 4 weeks and examined under microscope

## RESULTS

Both cellular and acellular corneas show radio activity in the stroma layer as shown by an increase in the silver granules over the sections

*Survival and growth of Descemet's membrane in the anterior chamber*  
 Descemet's membrane was obtained from cadaver and the endothelium was scrapped off. It was laid on filter paper and measured in millimeters. Then it was implanted into the anterior chamber of an absolute glaucomatous eye so that it had no contact with the host endothelium. It was observed from time to time by slit lamp for transparency and morphological survival. After three months it was removed from the anterior chamber, measured and histologically examined. It was found that it survived morphologically, although it lost about 25% of its transparency. But by measurement it had increased in size by a few millimeters. This experiment shows that Descemet's membrane is alive and viable membrane and can survive and even grow without endothelium.

The results of these experiments support observations in the clinics and histopathology. In the presence of the endothelium, Descemet's membrane can increase in length, reduplicate and curl after surgery or traumatic injuries. Thomas<sup>(9)</sup> mentions a histopathological report from a case of marginal degeneration of the cornea where Descemet's membrane has thickened and increased three to four times the normal, in the absence of the endothelium. It is also well known that Descemet's membrane in a descemetocoele is elastic when viable but disintegrates when it becomes necrotic. This shows that it can exist in two states, a living and viable state or a dead and necrotic state.

At several instances, Hogan and Zimmerman<sup>(6)</sup> describe collagen fibers of the cornea in a dead and/or necrotic state, presupposing alive or viable state. They mention that a degenerated structure is not in a dead state. So when the corneal lamellae and membranes are described to be degenerated, it implies that they are not dead structures but can exist in a viable degenerated condition.

## SUMMARY

Acellular human and fowl corneal grafts were produced by instantaneous freezing to  $-49^{\circ}\text{C}$  and leaving them or embryonating them in chicken eggs for 48 hours. For the first time acellular corneal grafts have been tried clinically in 26 lamellar and 2 penetrating keratoplasties. The overall results show that when the host is favourable in lamellar keratoplasty the acellular homograft maintains its transparency to an extent equal or in some cases better than the frozen dehydrated cornea of the World Eye Bank. Their transparent survival are similar to cellular graft. When the bed of the host is unfavourable with vascularization anterior synechiae, extensive leucoma or glaucoma they turn partially or totally opaque. Four fowl acellular heterografts became totally opaque and disintegrated although their survival was longer than the cellular heterografts. Two acellular lamellar homografts where the host beds were formalinized eventually disintegrated also.

The acellular cornea was found by the Warburg apparatus to consume oxygen under room temperature in NSS although to a lesser extent than when the cells were present. This shows some respiration of the non cellular portions of the cornea.

It was shown that acellular cornea like cellular cornea has the property of hydration at  $+4^{\circ}\text{C}$  and dehydration at  $+37^{\circ}\text{C}$ . This almost entirely disappears on soaking it in formalin. Acrylic plastic lens and gelfilm could not dehydrate themselves at  $+37^{\circ}\text{C}$ .

Incorporation studies have demonstrated that using  $\text{S}^{35}$  as sodium sulfate injected sub-conjunctivally *in vivo* that acellular cornea like the cellular can incorporate the radio-isotopes as shown by the Geiger counter and manifested radio-activity in the stroma layers as shown by autoradiography.

Implantation of Descemet's membrane without endothelium into the anterior chamber demonstrated that it can survive morphologically with some loss of transparency but with slight increase in size after 3 months.

Instances are cited from the literature where Descemet's membrane and stromal fibers can exist in a viable degenerated condition distinct from a dead or necrotic state.

## DISCUSSION

There is no definition of a living structure that is currently accepted by all because survival with life has been confused with propagation of life. It seems that with reference to a particular structure survival and propagation can not mean the same thing. If viability should mean the capability to survive with life then propagation or reproduction which is sometime used synonymously with growth is not a necessary condition in order that the structure should be viable. In tissue culture it is observed that cells can survive with life but stop multiplying if some essential elements in the culture medium are lacking. This is the concept of viability which we have followed in trying to answer the question: are the non cellular portions of the cornea viable?

In the cornea barely 10% of the 'formed structure' are cellular. Hence if corneal viability should refer only to cellular viability almost 90% of its structures — membranes and fibers would be considered dead. It seems therefore that corneal viability should refer not only to cellular but also to non cellular viability, although reproduction which is merely one of life's processes may be possessed only by the cells.

The concept that corneal viability is not essential to the maintenance of transparent survival in lamellar keratoplasty should be revised. It should state that corneal cellular viability is not essential but corneal non cellular viability is necessary for successful lamellar keratoplasty. It should also be made clear that the state of transparency is different from the maintenance of transparency. While the basis of the state of transparency may be morphological, physical, biochemical and optical for both inert and living structures the maintenance of transparency is biological in the viable formed structures but not in those which are inert. Hence if the biological processes are deficient the transparency of the viable non cellular portions of the cornea decreases or even disappears.

May be keratoplasty is the first kind of tissue transplantation where acellular graft has been tried. This may be followed in other

areas of tissue transplantation. An acellular graft is another approach and a further step in the study of transplantation allergy. Rejection of corneal homografts and heterografts should be differentiated from opacification with or without loss of viability and disintegration. The phenomenon of viability has received very little attention in the understanding of the many events of corneal grafting. It is time that viability should enter where allergy has heretofore been the sole consideration.

### CONCLUSION

There are sufficient clinical, pathological, biochemical, physiological and biological evidences that the non cellular formed structures of the cornea are viable in the sense that viability means the capability to "survive with life" with or without the property to "propagate life."

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## TRANSPLANTATION OF CORNEA IN CHILDREN

BARKHASH S A (U S S R)

Transplantation of cornea is an outstanding achievement of modern ophthalmology. This remarkable operation, however, is still rarely applied to children for fear of various complications related to their restlessness in the post-operative period. Besides that, it is somewhat difficult to perform this operation on a child under general anaesthesia.

We believe that this approach is incorrect. It is precisely children that should be restored to normal vision as early as possible. Besides that, a few years' postponement of an operation will make it almost useless, because the child will have developed grave amblyopia.

Five hundred operations of corneal transplantation on children aged between 6 months and 15 years were made at the children's department of the Filatov Institute.

The transplantations were partial though nearly complete as well as those made layer by layer. Sixty five percent of them were successful.

Here are the basic prerequisites of an effective grafting operation on a child:

- 1 Careful examination and pre-operative preparation of children
- 2 Proper selection of the surgical method.
- 3 Effective general anaesthesia
- 4 Prolongation of post anaesthetic sleep
- 5 Firm fixation of corneal grafts with a conjunctival band or corneal sutures
- 6 Use of tissue therapy and corticosteroids
- 7 Organisation of good care of children
- 8 Exercises to correct vision in amblyopic eyes

The following are the characteristics of the post-operative period: milder symptoms of allergic reactions, rarer occurrence of glaucoma and trophic disturbances, stronger optic refraction.

Our observations on corneal transplantation over the past 15 years prompt us to recommend its wider application to children with corneal opacities.



## GAMMA GLOBULINE, ENZIMES ET DIBAZOLE EN TRAITEMENT DE LA KERATITIS HERPETICA

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Jusqu'à présent on n'a pas trouvé les médicaments capables d'action  
virus statique sur l'agent de herpes cornéa simplex. C'est pourquoi  
en thérapie de la keratitis herpetica nous avons choisi la voie d'agir  
sur le système nerveux du malade compte tenu de propriétés neuro-  
tropiques de l'agent. A cet effet, nous avons administré le dibazole —  
sel chlorhydrique 2 benzile benzimidazole — qui est efficace lors des  
actions toxiques et infectieuses sur le système nerveux en remettant la  
sensibilité motrice, douloureuse et thermique après troubles mécani-  
ques du système nerveux, comme après l'effet de poisons, d'agents  
microbiens et virulents.

Dans nos expériences aux lapins, nous avons réussi de constater,  
que les injections prophylactiques du dibazole empêchent l'origine et  
développement de la keratitis herpetica expérimentale.

Injectons du dibazole aux lapins exercent une influence  
thérapeutique évidente. Les symptômes cliniques de la keratitis  
herpetica deviennent faibles et cessent au 10-11 jour de maladie  
au lieu de 17-20 jour chez les lapins sous contrôle.

Dibazole, ne s'exerçant sur le virus de herpes, augmente la  
réaction et résistance d'un microorganisme par rapport à l'agent  
seulement, c'est pourquoi, il faut l'administrer en combinaison avec  
la thérapie étiologique. A cet effet, nous avons appliqué le gamma  
globuline. Son application est affirmée par le fait, que chez la majorité  
de population adulte on trouve dans le sang un haut titre d'anti-  
corpuscules spécifiques en regard à l'agent de la keratitis herpetica.  
Formation de ces anticorpuscules capables à neutraliser le virus, est  
liée avec l'existence de la fraction gamma globuline de protéines du  
serum de sang. Concentration de ces anticorpuscules spécifiques en  
séries gamma globulines dépasse de 20-25 fois leur concentration  
dans le serum ordinaire de sang.

Le traitement était administré aux 60 malades aux formes diverses  
de keratitis herpetica. Les 13 malades avaient la souffrance primaire  
les 17 — les récurrences. Dibazole était administré aux 8 malades in-  
loco, sous forme d'une solution 1% par l'électrophorèse à l'oeil, les

autres malades recevaient ce preparat per os — II 02-0 03 trois fois par jour cette derniere methode de l'application du preparat se trouva la plus efficace

Le gamma globuline était administre in loco, car justement dans le foyer de trouble nous cherchions de creer la concentration maximum d'anticorpuscules. Le gamma globuline était instille dans l'oeil souffrant 6-8 fois au cours de 24 heures ou on en injectait 0.5 ml sous la conjonctive de la sclerotique, plus près de la section troublee. Ces injections étaient realisees chaque jour ou tous les deux jours en variant leur nombre total de 2 a 7 sous dependance de la gravite du procede

L'administration du gamma globuline se trouve surtout efficace dans les cas frais ou il y a la phase virucémique de maladie. Le mecanisme de penetration de la particule virulente dans la cellule n'est pas etudie jusqu'a present. On sait, que la penetration du virus dans la cellule commence par adsorption des particules du virus a la surface de cellule. Justement au cours de cette periode ci que les anticorpuscules commencent a s'exercer sur le virus. Les anticorpuscules serums de reconvalescents se repartissent a la surface de cellules susceptibles en y empechant la penetration du virus.

Chez malades dont la duree de souffrance ne surpassait pas trois semaines les sensations douloureuses dans l'oeil et photophobie se baissaient au 2nd ou 3me jour du traitement administre. Sensibilite de la cornee commençait a remettre les erosions herpetiques s'epitheliaient.

Dans les cas chroniques ou le virus s'est deja localise endedans de la cellule l'application du gamma globuline était precedee soit par administration soit par instillation de la solution 1% tripsine, dans le sac conjonctival. Tripsine comme possedant une action proteolytique donne lieu a destruction de proteines du virus, et alors il neutralise le virus en le preparant pour phagocytose. Nous n'avons constate aucun effet collateral du a l'administration du tripsine, car nous ne l'avons applique qu'en concentrations faibles et combine obligatoirement avec l'instillation du gamma globuline.

L'administration de preparats susmentionnes resultait en guérison des keratites herpetiques fraiches et chroniques aux troubles superficiels et profonds de la cornee.

Chez malades aux troubles de la cornee chroniques, c'est a dire hospitalises a cause de recidives de la keratitis herpetica, les procedes de reparation n'étaient pas si complets. Les procedes inflammatoires étaient coupes sensibilite de la cornee remise vaisseaux de cornee superficiels et profonds devenant vides — disparus mais les changements cicatrisants de la cornee restaient et la remise du visus chez ces malades n'était pas si complete que dans les cas frais.

En 91.3% de cas il y avait une guérison complete. Dans 5.7% il restait un stable trouble de la cornee.

En general, on sait, que les keratites herpetique ont une forte tendance aux recidives. En surveillant nos malades au cours de 1, 5-2, 5 anneés, nous avons constate seulement un cas de recidive. Il est evident, que dibazole en s'everçant sur la transmission acétyle choline de l'impulsion nerveuse et se trouvant en correlation positive avec la cholinergie, stimule la resistance d'organisme contre le virus et y empeche les recidives possibles.

## PHYLOGENY IN HETEROGENEOUS KERATOPLASTY

LALIT P AGARWAL A K GUPTA G C SOOD S R K  
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It has been suggested that opacification and vascularization of corneal grafts especially the heterografts are essentially dependent upon an antigen antibody reaction between the donor and recipient cornea (Babel and Bourquin 1952 Choyce 1952, Basu and Ormsby 1957) It has been pointed out that this donor recipient reaction is less marked the farther phylogenetically are the donor and the recipient (Basu and Ormsby 1957) It is also common knowledge that even autografts become opaque In all this assessment an important factor or hypersensitivity of the recipient has not been taken into account With a view to assess these factors the following aims were kept in mind by us

- 1 The relative antigenic properties of corneas of various species
- 2 The hypersensitivity of the host to the various antigenic corneas
- 3 The species specificity of corneal proteins,
- 4 Antigen antibody response to the antigens of corneas of various species,
- 5 The prediction of the end results of a corneal intralamellar graft on the basis of hypersensitive reaction and antigen antibody response

The above have been achieved by the following procedure

- 1 Experimental intralamellar grafting of cornea from various species into the rabbits eye
- 2 Response of human beings to corneal antigen from various species after intradermal injection
- 3 Electrophoretic studies of corneal antigen of various species
- 4 Agar gel diffusion study of antigen antibody response in rabbits after intraperitoneal injection of corneal antigen from various species
- 5 Intralamellar grafting in hypersensitive and insensitive rabbits and assessment of results

## I EXPERIMENTAL RESULTS OF GRAFTING FROM VARIOUS SPECIES

A series of experiments were carried out in which rabbit was used as a recipient and the donor material was taken from four different phylogenetic groups, Pisces (fish), Amphibia (frog, *Rana tigrina*), Aves (chicken) and Mammalia (goat and dog). Ten grafts were performed with material from each species except dog from which only two grafts were obtained. Full thickness 6 mm in diameter circular discs of donor cornea were grafted intralimellarily by the technique of Agarwal et al (1962) in all the experiments. One eye each from the first four series was enucleated one, two, four and eight weeks and three and six months after the graft and histopathological studies on them were done. The rest were clinically observed.

In this experimental study we observed that haziness of the graft occurring in the early postoperative period is mainly due to operative manipulations and was not associated with any ingrowth of blood vessels into the cornea. In eyes in which donor recipient reaction occurred the opacification of the graft appeared after one week and was always associated with invasion of blood vessels into the host cornea which in severe cases progressed into the donor tissue. In some eyes we observed that the reaction was quite intense in the host tissue which became markedly opaque, while the donor tissue was little affected and remained relatively transparent.

This probably was a hypersensitive response of the host to the donor tissue in which the former showed an excessive reaction while the latter was little affected.

This led us to believe that there are other factors besides the antigen antibody reaction which have profound influence upon the ultimate results of heterokeratoplasty.

From our experimental studies (clinical and histological) we learnt that the frog heterograft aroused least reaction in the rabbit (Figs 1 and 2) followed by chicken (Figs 3 and 4) and fish (Figs 5 and 6) respectively. The results were extremely poor in goat and dog series (Table 1 and Figs 7 and 8).

Our observations do not show exact correlation between phylogeny and opacification of the graft. Frog and chicken are phylogenetically nearer to rabbit than the fish and the better results with these species do not support the views of Basu and Ormsby (1957) and go against the theory of phylogeny in the success of heterokeratoplasty.

## II RESPONSE OF HUMAN BEINGS TO INTRADERMAL INJECTION OF CORNEAL ANTIGEN

### (a) Preparation of the corneal extract

The eyes were collected within 2-3 hours after the death of the animal and thoroughly washed with antibiotic solution. Corneas were excised and made into fine paste by grinding with glass powder care being taken to keep the temperature as low as possible during the whole process to avoid denaturation of proteins. An equal amount of

TABLE I—End Results of Intraocular Heterografts

Series	No of eyes	Opacity		Results +++	Extruded corneas	Clear corneas
		+	++			
Fish	10	4	5	1	1	—
Frog	10	—	—	—	—	10
Chicken	10	6	2	—	1	1
Goat	10	5	1	3	1	—
Dog	2	—	1	1	—	—

The results were read as follows

+ (One plus) When the opacity was slight and was seen with difficulty with the naked eye. It was more obvious with slit lamp examination. Iris and pupil was seen easily through the haziness.

++ (Two plus) The opacity was moderately dense. Iris and pupil was seen but details were not possible.

+++ (Three plus) The opacity was dense and pupil and iris could not be seen through it.

sterile normal saline was added and the whole thing was left for 48 hours at 4°C. Centrifuging under refrigeration was done at 10 000 revolutions per minute for 15 minutes. Clear supernatant fluid was dialyzed against distilled water to remove excess of salts. The extract was concentrated by evaporation technique till the protein concentration rose to about 3% as determined by biurate method. The extract was filtered through Seitz filter and its sterility was confirmed by negative culture.

Corneal extract was prepared with the corneas of four species i.e. goat, fish, chick and frog.

#### (b) Intradermal test in human beings

Intradermal tests were carried out in human beings by injecting the corneal extract of four different species mentioned above. The extract was injected in the forearm skin so as to raise a wheal of about 4 mm size. Normal saline was injected as a control in the opposite forearm. The reaction was read after 24 hours, 48 hours and 72 hours (Table II).

These tests indicate that human beings show a varying degree of sensitivity to corneal antigens derived from various species. The antigens from the frog cornea show the least response followed by chick, fish and goat. They do not show any correlation to phylogeny. To 50 adult human beings of about 40-45 years of age in the right forearm intradermal injection of corneal antigen from all the four species was

TABLE II — Intradermal test in Human beings

Animal	Total No of cases	Total No of cases showing +ve reaction	Degree of reaction		
			+	++	+++
Goat	50	24	3	18	3
Fish	50	9	5	4	—
Chicken	50	8	5	3	—
Frog	50	3	2	1	—

Note

+ Erythema more than 5 mm Induration less than 5 mm

++ Induration 5 to 8 mm

+++ Induration more than 8 mm

given. A wheal of 4 mm was raised by the antigen of each species separately. The wheals were separated from each other by an interval of two inches. Similar four wheals were raised in the left forearm by intradermal injection of normal saline. The results are given in (Table III)

TABLE III — Response of human volunteers to various corneal antigens

S. No.	Number of cases (Total 50)	Frog	Fish	Chicken	Goat
1	1	+	+	+	+
2	2	+	—	—	—
3	10	—	+	—	—
4	2	+	—	+	—
5	2	—	+	—	—
6	2	—	—	—	—
7	2	—	+	+	—
8	14	—	—	—	—
9	15	—	—	—	—

These results indicate that each individual is not sensitive to the antigens from all species. This suggests to us that corneal antigen may be species specific and not organ specific. This also gives an indication of probable choice of donor material.

### III. ELECTROPHORESIS OF CORNEAL PROTEINS

Paper electrophoresis of the extracts from the cornea of different species was done on Whatman paper No. 1 using barbitone buffer

ph 8.6 molar strength 0.1 at 150 volts for 18 hours. Number of bands obtained and their percentages are given in table No. IV and Fig. 9.

TABLE IV. — *Electrophoretic patterns of corneal proteins from various species as compared to human serum*

	Albumin	Globulin %			
		Alpha 1 %	Alpha 2 %	Beta %	gamma %
Human serum	57.33	3.86	8.50	13.75	16.50
Goat corneal extract	6.31	—	12.13	19.41	62.15
Fish corneal extract	—	—	22.34	27.10	50.56
Chicken corneal extract	40.28	—	—	35.13	24.57
Frog corneal extract	—	47.14	—	35.72	17.14

These bands and their relative percentages indicate that the nature of proteins of cornea of various species differs considerably. These differences may be responsible for species specificity of these proteins. The higher the gamma globulin percentage the more reaction it produces. The content of gamma globulin in frog's cornea is very near the gamma globulin content of human serum. This may be a factor accounting for its low antigenicity to human beings.

#### IV. ANTIGEN ANTIBODY RESPONSE TO THE CORNEA OF DIFFERENT SPECIES

Immune sera were obtained from rabbits after sensitizing them against the corneal extracts of above mentioned four species. To achieve this intraperitoneal injections of corneal extracts were given twice weekly in increasing amounts (0.2 cc, 0.2 cc, 0.4 cc, 0.8 cc, 1 cc, 1.0 cc, 2.0 cc, 2.00 cc). Three rabbits were sensitized against each species. Quantitative estimation of antibodies was done by microprecipitation technique. The positive titres were as follows:

Goat 1:32, Fish 1:8 and Chick and Frog 1:4 (Fig. 10).

The presence of antibodies was further demonstrated by agar gel diffusion technique. One per cent agar gel was prepared in normal saline. About 4 cc of this was put on a slide and allowed to set. Bottom of the holes were sealed by gently warming the slide. Antigen was



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3	10	—	—	—	+
4	2	+	—	+	—
5	2	—	+	—	+
6	2	—	—	—	—
7	2	—	+	—	—
8	14	—	—	—	+
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put in the central hole and antisera in the peripheral holes. The results are as in Table V.

TABLE V — Results of Agar gel diffusion technique of demonstration of antibodies

Animal	Number of bands Antigen and Immune serum	Control Antigen and Normal Serum
Goat	3	nil
Fish	2	nil
Chicken	2	nil
Frog	2	nil

### INTRADERMAL TESTS

With goat and frog corneal extracts intradermal tests were carried out in rabbits. It was observed that in the goat series 8 out of 10 rabbits showed positive reaction. In two rabbits the reaction was necrotising and in 5 it was +++ and in one it was ++. In frog series only three rabbits out of 8 showed positive reaction. In 1 it was +++ in the remaining two it was ++. Keratoplasties were performed both on sensitive and insensitive rabbits.

### RESULTS

Frog series — Except for one (with +++ reaction) all other grafts remained transparent.

Goat series — In all cases there was intense reaction resulting in opacification of the cornea. Blood vessels could be seen in the host tissue towards the graft on the 6th and 7th postoperative day. This vascularization persisted though its intensity started diminishing after 15-20 days. The graft remained opaque in all these cases.

These results indicate the possibility of an intradermal test as a means of predicting the site of the graft, as well as the choice of the species. The work is still in preliminary stage and has to go a long way before it can be established as a procedure. It is being extended to the monkeys and the results will be awaited with considerable interest.

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## LAMELLAR KERATOPLASTY IN CORNEAL FISTULA

RAIS, HADI and YOUNG (TUNISIA)

The fistula of the cornea is a characteristic affection in countries where TRACHOMA CONJUNCTIVITIS ASSOCIATE exist, particularly in Africa and Asia. Only a tectonic Keratoplasty can spare the panophthalmia which is a major complication.

But the presence of flattened camera aquosa is a difficult problem. If the keratoplasty is considered as being the major indication for the treatment of the corneal fistula, the authors are not agreed for the technique employed. We propose the lamellar keratoplasty as being the proceeding more indicated above all when there is a flattened camera aquosa. We have treated by this technique thirty cases successfully.

## FUNCTIONAL DETERMINISM OF THE CORNEAL BIO ARCHITECTONICS IN PARTIAL KERATOPLASTY

MIHAI CARAPANCEA

However thoroughly the technical conditions of any of the numerous operative variants known to day in partial keratoplasty are observed, they yield quite unreliable results, even at the hand of the same surgeon ophthalmologist. Either the minute portion of the cornea remains definitely transparent or, after several days or several months, it becomes more or less cloudy or even opaque.

As all biological hypotheses regarding the failure of the operation have been invalidated, there is at present no criterion by which the maintenance of the transparency of the corneal transplant can be predicted.

The success of the implantation of a portion of tissue into a histologically similar tissue depends upon the rapid adaptation of the implant to the medium of the host tissue.

The rapidity of the adaptation is, however, conditioned, to a certain extent by the evolutive stage of the specialization of the respective tissue. It is well known that tissues, less developed in their specialization, adapt themselves more readily than those which are more highly developed, such as the cornea.

The cornea, a small skin fragment — the ectodermic derivation rendered transparent, is an evolutionarily differentiated tissue, as a consequence of local stresses determined by functional necessities of the visual apparatus.

In conditions of the slow adaptation of the corneal transplant to the new environment — host corneal medium, — the corneal graft retains for some time its unmodified biological personality, as it cannot integrate itself into the neighbouring biological atmosphere. In the meantime irreversible regressive modifications with respect to the normal take place in the cellular functions of the transplant, as it is expressed by the variable clouding of the corneal graft up to its complete opacification.

Thus, though two similar tissues with identical biological history have been brought into contact, — an actual *in vivo* culture being achieved, — the survival in a live medium practically similar to that from which it originated — the biological harmony not taking place *in due time*, it has rendered priority appearance of irreversible

degenerative modifications in the cellular functions of the corneal transplant possible, as it is shown by the loss of transparency in the transplant (2)

In the long run the adaptation of the transplant to the new corneal environment takes however place, even in the imperfect conditions of complete opacification of the transplant since the corneal graft is not eliminated as a foreign body, as would happen in the case of a complete inadaptation of the transplant

My new explanation of the degree of opacification of the transplant and the corrective I consequently suggest are based on the principle of the adaptation of the corneal graft to the new medium of the host cornea in conditions of strict observance of the natural functional bio architectural structure of the cornea

The cornea is a transparent epithelio conjunctival membrane the cellular elements of which form six symmetrically disposed layers namely peripherally two epithelial layers of which the more important anterior one is placed on the layer of a fine basal membrane of its own then internally, two lamellar layers, and centrally the layer of its own cellular fibro elastic material which contains the lymphatic lacunar system

Thus the natural functional structure of the cornea consists in there six corneal lens layers — with their arrangement in the shape of spherical segments moulded over each other, in their arrangement of alternating thicknesses and in the alternating differences in certain layers in the thickness between center and periphery — are nothing but the directed trabeculae of the biological lines of force representing the expression of the organized materialization of the component cellular elements considered in their aggregate grouping

In fact the cornea only represents the natural functional bio architectural systematization resulting from the organization of its cellular elements in conditions of existence of the determinism expressed under the aspect of two general structural patterns — a bio mechanical pattern in corneal layers and a bio optical one in corneal lenses (1)

The mechanical bio architecture of the corneal layers has the following characteristics

- 1 The convexity of one layer fills the corresponding concavity of the immediately anterior layer (Diagrams 1 2 and 3)
- 2 The layers include in the middle their own cellular material (90% of the entire corneal thickness) like a thick cemented pillar (Diagram 3)
- 3 The thickness of the layers are disposed alternately balanced in the following way the anterior epithelium (layer 1) is by 3 60% thicker at the periphery than in the center, the basal membrane (layer 2) is by 0 15% thicker at the periphery than in the center the Bowman membrane (layer 3) is by 0 82% thicker in the center than

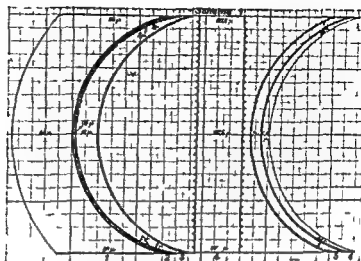


DIAGRAM 1 Diametral section of the cornea with the thickness of the component layers  
1-6 Layers of the cornea

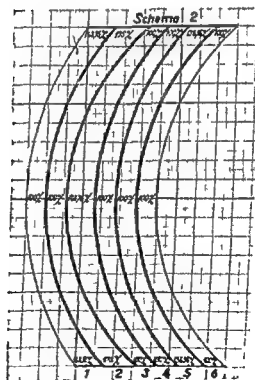


DIAGRAM 2 Diametral section of the cornea with the thickness differences of each layer in percentages to its own thickness  
1-6 Layers of the cornea

at the periphery, while the Descemet membrane (layer 5), by 0,32% thicker at the periphery than in the center, is comprised between two

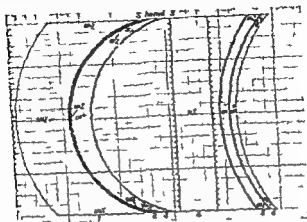


DIAGRAM 3 Diametral section of the cornea with the thickness of each layer in percentages to the total thickness of the cornea

1-6 Layers of the cornea

layers both identically thick over their entire extent in front its own cellular material (layer 4) represents 90% (layer 6) and behind the posterior epithelium 60% (layer 3)

4 The disposition of the thickness of layers and their orientation in their totality make out of the membrane — provided with a mechanical and statical function of enveloping and containing the anterior part of the eyeball — a more resistant architectural whole than if the cornea was a simple band made up of a single tissue of the same total thickness as that of the six component layers (Diagrams 1 2 and 3)

*The optical bio architecture of the corneal lenses has the following characteristics*

1 The corneal layers are transparent

2 The convex concave shape of the layers in their above described alternating thickness confers them the value of irregular convex concave lenses (layers 1 2 3 and 5) and of regular ones (layers 4 and 6) (Diagrams 1 2 and 3) the value is however only theoretical as the layers being histologically welded together, they practically form a convex concave dioptric system the corneal lens in the shape of a convergent meniscus thicker by  $33.5 \mu$  at the periphery than in the center (Diagram 1) in which refraction occurs at the level of the anterior surface of the anterior epithelium and of the posterior surface of the posterior epithelium



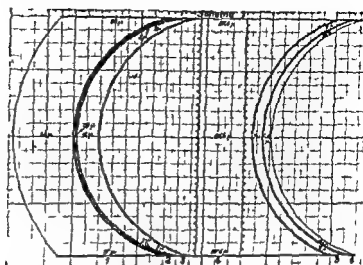


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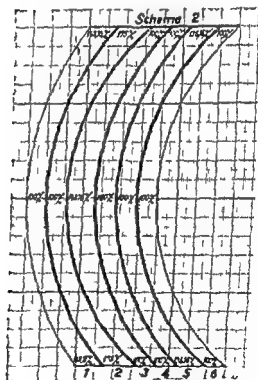


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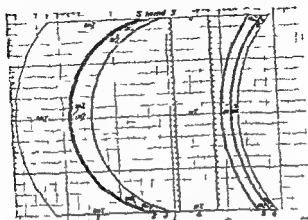


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*The optical bio architecture of the corneal lenses has the following characteristics*

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2 The convex concave shape of the layers in their above described alternating thickness, confers them the value of irregular convex concave lenses (layers 1, 2, 3 and 5), and of regular ones (layers 4 and 6) (Diagrams 1, 2 and 3) the value is however only theoretical as the layers being histologically welded together, they practically form a convex concave dioptric system the corneal lens in the shape of a convergent meniscus thicker by  $33.5 \mu$  at the periphery than in the center (Diagram 1) in which refraction occurs at the level of the anterior surface of the anterior epithelium and of the posterior surface of the posterior epithelium

The above facts show that the explanation of the situation of the opacified (leucomised) transplant must be looked for in the non observance by the graft of the host corneal bio architecture, in other words in the intercellular fusion of the layers if the two corneae which do not comply with normal histology, without observing the identity dualism of a corneal graft layer towards the same corresponding layer of the host cornea, thus not respecting either the local metabolism of the two corneae brought into contact with each other

The functional — anatomical realities of tissues in general are undoubtedly also based on the respective unquestionable local metabolisms which are however, still unknown to us in their immense complexity. Particularly in the case of corneal metabolism, many anabolic and catabolic functions undoubtedly intervene, functions which are just as delicate as that fulfilled by this transparent film of the organ of vision

As the layers of the transplant do not correspond to the anatomical continuity of the surrounding corneal layers, not being in contact with one another, they will find themselves facing different layers each having its own physiology. Hence the imperfect interaction of the functional anatomical relations between the biological processes of the two corneae brought into contact, and no harmonious whole in its general physiology will therefore be formed

The fact has generally been observed, without any explanation being given, that the transparency of the transplant is more often ensured if the leucoma is completely extirpated, down to the normal tissue, than if the transplant is placed into a leucomatous tissue. In other words, it is obvious that the chances of maintaining the transparency of the transplant are greater if the bio architecture of the host cornea is at all observed. On the other hand the occasional achievement of the histo architectural harmony between the layers of the two corneae explains the variable proportions of successful operations by the same surgeon

Partial keratoplasty, as practised to day puts two similar tissues into contact, but *by no means* two similar structures, so that the biological properties of the transplant layers will finally coincide only along general lines with those of the layers of the host cornea. Hence it will result in a general adaptation of cornea to cornea but by no means a detailed adaptation of corneal layer to corneal layer. In this case the viability of the new corneal entity will be ensured only in conditions of cloudiness resulting from low biological exchanges with the surrounding cornea at this level. Thus, as the corneal lens layers of the transplant do not find similar histo functional correspondents in the neighbouring layers of the host cornea — i.e. they cannot adapt themselves to the corneal graft medium — a corresponding degree of reduction of the transplant transparency sets in, in proportion to the metabolic disturbances of the consequent development of the conjunctival tissue

The various degrees of cloudiness and opacification mean, therefore the expression of imperfect mutually harmonious relationships between transplant and the neighbouring cornea.

The striking fact however is that, whatever the degree of its cloudiness the transplant should remain more or less independent and isolated retaining its biological personality even in the midst of the same material which it is made itself of. The maintenance of its personality also depends undoubtedly to some extent upon the subsequent state of neurovegetative correlation — consisting of the regeneration of the nervous fibres — a very difficult process of anatomical restoration. In this connection it is of interest to note that 17 days after transplantation the corneal graft presents a well defined sensitivity in its most peripheral portion (Jorn Boberg Ans), a situation which is in concordance with the general topography of the normal corneal sensitivity which presents a localisation all the more difficult as it approaches the central portion of the normal cornea.

The biological aspect of the enclavement of the transplant should however also be considered from the point of view of the host cornea. In other words a foreign normalizing state occurs in the region of the bed of the former leucoma in the place in which the host cornea was adapted to an abnormal state of its own. One may therefore speak of a readaptation to normal conditions for the host cornea in the region of the extirpated leucoma and of a biological integration for the transplant.

The structural reality of the cornea thus imposes the notion that since the layers of the cornea vary according to the region involved only the observance of the local bio architectural concordance between the two corneae in contact with each other can guarantee the perfect functional integration of the transplant into the host cornea in the sense that only the correct histological unification of the corresponding layers of the transplant and of the host cornea can guarantee the maintenance of the transparency of the transplant.

The morpho functional bio architectural concordance between corneal graft and host cornea imply necessarily the following conditions

- 1 The transplant should have a topographical situation on the cornea from which it was taken identical with that of the leucoma in the cornea from which it was extirpated,
- 2 The orientation of the transplant should be identical at the site of the lack of material in the host cornea with that in the place from which it had been extirpated
- 3 The transplant should have an identical curvature with that of the host cornea which implies the same slope in the corresponding cellular planes as that of the per transplantic layers
- 4 The transplant should have its cellular layers of an identical thickness as that of the corresponding ones of the host cornea which

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implies the same age of the transplant as that of the host cornea, and, at the same time, the bringing into contact of two similar biological forces

In partial non penetrating keratoplasty, the basal layer of the transplant should be, in conformity with normal histological alteration, immediately above the layer constituting the bed of the host cornea. Therefore the simple quantitative replacement of the leucoma by a transplant of the same thickness is inadequate, since in practice the thickness of the cloudy, infiltrated corneal layers, thickened by the conjunctival tissue of the leucoma, corresponds to a much smaller number of transparent corneal layers of the transplant,

5 The transplant should have as small a surface as possible in order to observe the configuration in depth of the layers of the host cornea, since the more extensive it is, the less it will observe the configuration in depth of the layers of the host cornea

### Practical Conclusion

The transplanted cornea should replace the leucoma in identical functional, structural conditions with those of the host cornea at the place of the extirpated leucoma, so that the local observance of the general dispositions of the biological lines of force materialized in histo architectonically organized trabeculae of the two corneas brought into contact, i.e. the inter corneal morpho functional bio architecture, should form a non differentiated and isorefringent vital whole

The Laboratory for Clinical and Experimental Eye Physiology of the Normal and Pathological Physiology Institute "Daniel Danielopolu" of the Academy of the Rumanian People's Republic  
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## ARTIFICIAL EPISCLERAL SCHLEMM'S CANAL FOR JUVENILE CONGENITAL GLAUCOMA

DR B L PANDE

Ophthalmic Surgeon, U H M Hospital Kanpur (U P)

The modern conception about the pathogenesis of juvenile and congenital glaucoma is a maldevelopment at the angle of the interior chamber mostly maldevelopment of the Schlemm's canal leading to defective drainage of the aqueous humour from the anterior chamber.

Goniotomy Operation which is the operation of choice in such cases requires costly equipment like the gonioscope etc to achieve ultimate success.

The few cases of goniotomy or even those supplemented with Gonipuncture in juvenile and congenital glaucoma I have come across have not impressed me at all. Perhaps Goniotomy is not able to correct the deficiencies and defects of Schlemm's canal it can only correct those defects which are limited to the angle of the chamber (Anterior). I have therefore adopted the following surgical procedure for these cases which have given good results in my hands.

I take the conjunctival flap (Fig 1) along with the sub conjunctival tissue as in sclerocorneal trephining or iridencleisis from 3 to 9 o'clock (upper half circumference of the limbus) and dissect it with the Langs or Fooke knife as far forward over the cornea as possible. Then I insert three episcleral silk sutures (Fig 2) at 12 o'clock 10 o'clock and 2 o'clock as far forward as possible near the limbus making allowance



FIG 1



FIG 2

for the Keratome incision at the limbus to open the anterior chamber just in front of these sutures a keratome incision is made and enlarged with Castroviejo corneal scissors to complete the opening from 3 to 9 o'clock.

Then a big 8-10 mm or three small pieces of 3-4 mm elliptical piece of tarsus is or are taken from the patient's upper lid if it is healthy and nontrachomatous otherwise a big 8-10 mm or three small pieces of



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Two cases will illustrate the points — (1) Mr Z a case of absolute glaucoma was operated in July 1957 for his right eye Tarsal plate from his own upper lid was grafted Before operation the right eye tension was 55 (Maclean's tonometer) After operation tension came down to 30 Maclean's which was again checked after 2 months in the first week of September and found to be the same

(2) Mrs R admitted on 28th July 57 discharged on 23rd August 57 Juvenile glaucoma of the left eye Tension 33 mm Hg before operation right eye ulcer cornea resulting from phlyctenular keratitis Cartilage from the left ear was grafted and tension came down to 15 after operation The patient did not come back for a check up of the progress obviously because there was no need the result of the operation having given her permanent relief

### Supplementary Data for Artificial Episcleral Schlemm's Canal in Juvenile and Congenital Glaucoma

Further following four cases were selected for the experiment besides two already quoted

Due to anterior synechiae the angle was blocked in all cases almost all around the limbus which was not much disturbed simply to observe the effect of the operation (except in case of No 3 at the cyclodialysis operation alone) or in all cases whatever anterior synectomy happened to have been automatically done while making a limbal section They were all cases of absolute glaucoma but with intact ciliary body function

### CASE NOTES

#### (3) P R S SECONDARY GLAUCOMA AFTER CATARACT EXTRACTION

Angle of the anterior chamber was altogether blocked all around simulating juvenile glaucoma In 1959, Cyclodialysis (transcleral) was performed and tension remained controlled for one year In 1960 tension again shot up to 55 mm Hg Schiotz and could not be controlled by repeating cyclodialysis Ultimately the artificial episcleral schlemm's canal was made and tension is all along controlled till now

#### (4) A S ABSOLUTE GLAUCOMA

Angle blocked all through in right eye by multiple anterior synechiae Admitted on 7th December 1960 operated on 13th December 1960 discharged on 24th December 1960 Tension before operation 60 mm Hg Schiotz Tension at the time of discharge 30 mm Hg Schiotz Tension one week after being discharged 23 mm Hg Schiotz

#### (5) MRS S W CASE OF APHAKIA RIGHT EYE

Operated for traumatic cataract at the age of 9 years In 1959, at the age of about 35 years developed glaucoma in this eye and was trephined for the same on 10th December 1959 Tension persisted hence cyclodialthermy as performed on 6th January 1960 with no

3-4 mm piece of cartilage from the external ear is or are taken and fashioned to suit the curve of the limbus. The width of the piece or pieces should be about 3 mm or so and the anterior concave side of the piece should be thinner than the posterior convex side.

After turning the conjunctival flap over the corner, the piece should be adjusted and fixed over the sclera at the site of the sutures by means of the latter which are brought above the piece in the centre of its width at these three places (12, 10 and 2 o'clock). As in (Fig 3). The sutures are not tied at this stage but are brought above the corneo conjunctival flap almost at the junction of conjunctiva with the corner by entering the flap from underneath as in the case of the tarsal or cartilage plate and tied over there (Fig 4). The

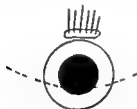


FIG 3



FIG 4



FIG 5

conjunctiva is sutured with continuous sutures (Fig 5). The usual dressing is done daily or on alternate days and the sutures removed after about a week.

### PRECAUTIONS

Before taking the sutures over the conjunctiva at the limbus from underneath, the flap of the latter should be stretched thoroughly well above towards the forehead so that (i) the sutures are fixed almost at the junction of the corneo conjunctiva and (ii) the plate keeps the anterior chamber slightly open by keeping away the corner from coming in contact with the cut scleral margin.

*Advantages* This operation requires very little or only cheap equipment as compared with the goniotomy operation and the results are much better and permanent.

### *Disadvantages*

- (1) It is more time consuming and
- (2) needs greater technical skill

**NOTE** Two narrow strips (each 1 mm wide) are cut out from the width of the plate at 11 o'clock and 1 o'clock after fixing the plate on the sclera by sutures it might prove a still better filtering channel and a genuine Schlemm's canal, though personally I have not yet tried it so far. Two deep grooves at these two places in the plate made by a sharp cataract knife might serve the same purpose as taking out of the strips.

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## **PATHOGENIC TREATMENT OF GLAUCOMA**

**Prof KHAYUTIN S M (USSR)**

Investigations which have been carried out for many years in the eye clinic of the Yaroslavo Medical Institute in the USSR have confirmed that glaucoma is the sequel of prolonged lesions of metabolic processes in the eye. These lesions may occur in consequence of injury of nervous elements of the eyeball, optic nerve and central nervous system. The first manifestations of these lesions appeared as pathological fluctuations of intraocular tension. The latter may be caused by local congenital and acquired alterations.

The changes in the regulation of the intraocular tension may occur as a result of local and systemic disease or injury which influences the normal functioning of the nervous system, anoxia in anaemias, cardiovascular diseases and endocrinal disorders, toxic action of products of metabolism in chronic gastro intestinal diseases, diseases of liver and kidneys, changes in the structure and function of the central nervous system due to trauma, changes in the efficiency of brain cells due to permanent overworking or mental trauma etc.

High prevalence rate of glaucoma in aged persons whose brain cells efficiency is rather often decreased, occurrence of glaucoma in cases with mental trauma as well as the finding regarding the action of pentothal sodium, aminatin, novocaine etc. confirmed the considerable role of the functional capacity of the central nervous system in the regulation of intraocular tension.

Our investigations of different degree of decrease of the intraocular pressure in the eyes of the same glaucoma patient subject to barbiturates and neuroplegic drugs and to the stage of the disease and its compensation have shown the importance of local changes in the pathogenesis of glaucoma.

Clinical and experimental investigations have shown that local effect of miotics and other drugs depends on the type and size of the lesions in the glaucomatous eye as well as on the functional capacity of the patients' nervous and cardiovascular systems.

Treatment of glaucoma should be aimed at the removal of the lesions which deteriorate the nervous activities, in particular of the reflex arc regulating the intraocular tension. The treatment should be aimed also at the improvement of metabolic processes in the eye to prevent further deterioration of the vision. It may be achieved by the removal of unfavourable factors influencing the functional capacity of the nervous system. Besides the removal or decrease of the influence

effect All the above operations were performed outside as stated by the husband of the patient On March 2, 1961, I examined the eye and tension was found to be 50 mm Hg Schiötz with no vision This operation was done on 24th March 1961 Right eye tension on 8th April '61 40 mm Hg

Pilocarpine and massage was prescribed on 8th May '61 Tension came down to 35 mm On 15th October '61 Tension was found to be 38 (*patient stopped pilocarpine and massage since one month*) On 14th November 1961, tension was again felt and it was found reduced to 33° Advised to continue pilocarpine and massage

(6) H P SECONDARY GLAUCOMA WITH NO VISION IN LEFT EYE

Angle blocked allround Tension 32 is given to me on 10th April '61 operated on 11th April '61 (taken at L L R Hospital) and tension checked on 30th April, 1961 found to be 16 mm Hg Subsequently, the tension was checked again after two months, and was found to be the same She had once been operated for glaucoma for this eye some years back by some one else locally and had some vision before operation

The right eye was trephined by me in 1959 for chronic simple glaucoma and she is seeing with the same eye

Tension again checked on 19th November 1961 which remains as before

NOTE If this operation is supplemented with anterior synechotomy or transcorneal cycloablation (Princk — 1956 A I O S Proceedings) it would give better results It would be most beneficial for cases like No 5 where the tension has not touched normal after operation though remains controlled

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at the factors like infections, autointoxication, alteration of oxidizing processes, etc., it is necessary to improve central nervous function in using suitable treatment programmes.

It was found out in our clinic that intravenous and periorbital injection of novocaine improved the absorption of the tissue fluids, slightly decrease the blind spot usually enlarged in glaucoma patients and improve the nourishment of the retina. Novocaine also strengthened the local action of the miotics.

A special attention should be paid to the hemodynamics. The changes of the vascular wall, contraction of arterioles and other vascular pathology gradually deteriorated the processes of metabolism. In such cases, the treatment should be aimed at the decrease of abnormal blood pressure. The attention of the ophthalmologist should be also paid to the cases with arterial hypotensions which may often lead to the decompensation of the glaucomatous processes in the patients with relatively mild intraocular hypertension.

It is also necessary to keep in mind other signs of hemodynamics as intravenous tension, speed of the bloodstream, the data of ECG, etc. Because of the increase of the prothrombin index in many of glaucoma patients we have applied anticoagulants to facilitate the bloodstream, to prevent the thrombosis of venules and to improve the eye metabolism.

The treatment of arteriosclerosis and gastro intestinal disorders, prescription of drugs to improve the barrier function of the liver, etc. is also very important. Endocrine therapy, properly applied, may have considerable influence on the course of the disease. Spring regime, vitamin rich diet, periodical taking of iodine and salicylate, mild sedatives and soporifics, oxygen and novocaine, while improving the general state of the patient may improve the condition of his eyes.

Local treatment of glaucoma should include improvement of the blood circulation, circulation of the aqueous humor, increase of oxidizing processes. The local treatment should be combined with systemic treatment.

Surgery should be recommended in early stage, in cases with congenital lesions or sequel of inflammatory or dystrophic processes causing narrowing or obliteration of the angle of anterior chamber and other changes disturbing due outflow of aqueous humor which cannot be improved by miotics and diuretics.

The operation should help to eliminate the causes of hindering the outflow of aqueous (goniosynechiae anterior and posterior synechiae, changes of the trabecular net of the angle of the anterior chamber and of the lens position, cataract, etc.). The surgery includes trabeculotomy, the operation performed in our clinic.

The operation, the description of which, was published for the first time in June 1960, consists in the routine separation of the bulbar conjunctiva, incision of the sclera near the limbus and insertion of the

eye spatula or trabeculotome in the anterior chamber. By rotating the trabeculotome along the chamber angle for a distance of 90-100 degrees the surgeon separates the trabeculae and destroys the existing goniosynechiae. In case of shallow anterior chamber, narrow or closed by iris angle, partial or full pupillary block trabeculotomy has to be performed with external iridectomy.

In late stages of glaucoma particularly in cases with rubeosis of iris thrombosis of the retinal vein as well as in cases of hypersecretion we perform the deep cyclodiathermy-coagulation. Unlike the other methods of cyclodiathermy coagulation we try to avoid the coagulation at sclera because it may lead to its shrinkage and may favour the increase of intraocular tension.

However these operations and the operations which help to form additional ways for outflow of aqueous and to improve the circulation of the aqueous, do not sufficiently normalise the metabolic processes. The quantitative and qualitative composition of aqueous apparently is not sufficient for the eye tissue nutrition in the majority of the glaucoma patients who were operated. This assumption is confirmed by the speeding up of cataract development and by further decrease of eye sight in spite of normalisation of the intraocular tension which is rather often observed after the performance of filtering operations.

The treatment of glaucoma patients should be continued in spite of the normalisation of the tension. Local treatment with miotics, particularly with pilocarpine, which improves blood and lymph flow inside the eye treatment with mesaton vitamins iodine and other drugs is indicated in cases where the intraocular tension reached the normal level after the operation.

Therapy should be changed according to the general condition of the patient and clinical course of glaucoma. It should be taken into account that the ability of glaucoma patients to the adaptation of the environment is not sufficient. The glaucoma patients therefore should be advised to stay in better climatic and environmental conditions.

Dispensatisation of glaucoma patients in our country provides the opportunity to follow up of the patients after the operation and to restart the treatment of those whose visual function decreases again due to various unfavourable factors.

## TOXIC TETRAETHYLELEAD GLAUCOMA

### Clinical and Experimental Data

Z. M. SKRIPNITSCHENKO

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Director—acad. N. A. Poutschkovskaja, Senior Scientific Collaborator,  
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Studying the state of organ of vision in persons dealing with tetraethylead and ethylgasoline we revealed a number of pathological changes. Clinical manifestations of these changes were due to the affection of neurovascular apparatus of the eye.

While carrying out prophylactic investigations of worker's eyes at the length of 5 years neither amaurosis or marked fall in visual acuity were recorded, and changes in peripheral boundaries of field of vision were absent as well.

Studying the eye vessels we observed the dilatation vessels at choroidal vessels and limbus to be present in some persons in particular, in those staying for long terms at factories. Separate vessels grew over the corner and branched out from periphery into its superficial layers. The diameter of vessels along their stretch was not equal. Here and there their scanty dilatations could be seen. Changes in the vessels of retina were revealed as well. The contraction of the artery was a characteristic feature in case.

In comparison healthy persons with those being in contact with tetraethylead the tension in the central artery of retina was increased. While measuring it by Brillhart its average made up 50.8 mm Hg, thus exceeding that of healthy persons (40-45 mm Hg).

In most persons under investigations the difference in tension of central artery of retina and inside the eye was great (20.0-45.0 Hg). According to Lauber (1936) this difference about 20.0 mm Hg is considered to be sufficient to secure normal blood supply of retina and optic nerve.

Kushuk M. E. (1938) proved the difference in tension of 13.0 mm Hg not to affect blood circulation in the vessels of retina.

The presence of regional hypertension in eye vessels and great difference of both pressures (of eye vessels and ophthalmotonus) can explain the fact that in case of high level of intraocular tension the visual acuity does not decrease and the field of vision and other structures of the eye do not suffer.

The dilatation of angioscotoma is another proof of the presence of the affection of retinal vessels. In some of the persons observed angioscotoma had the form of either a half moon or that of closed rings situated paracentrally, thus reminding typical Bjerrum scotomas.

The dilatation of angioscotoma often was combined with the contraction of retinal vessels and increased intra ocular tension.

While carrying out prophylactic observations the character of ophthalmotonus control was studied by Filatov half elastometric method. Intra ocular tension was taken by Maklakov's tonometer of different weights: 5.0, 7.5, 10.0, 15.0 gm. The normal limit for ophthalmotonus was considered to be about 28.0 mm Hg while taking its measurement with tonometer with 10.0 gm weight.

Controlled investigations of healthy persons revealed the threshold of elastometric curve in norm to vary from 12 to 20 and very rarely to be equal to 22 mm Hg. The level of ophthalmotonus was within 16.0—26.0 mm Hg. The rise in curves varied from 7 to 12.0 and rarely it was defined as high as 6.0 or 13.0 mm Hg.

All these elastometric curves had the form of ascending line, the break of curves was not noted. The data obtained concerning the norm of elastometric curves conform to available data of other authors.

In patients dealing with tetraethylead and ethylgasoline the normal type of elastometric curves was observed. High threshold of curves (above 22.0 mm Hg), the increased level of intra ocular tension (above 28.0 mm Hg), the break of curves and the change of their ascension were noted. In most cases the ascension of curves was above 13.0 mm Hg, thus determining the long type of curves.

High threshold of elastometric curves, ascension of ophthalmotonus level and long type of curves are characteristic for the clinic of primary glaucoma. Changes in elastometric curve reflected the inhibiting character of the process that developed under the influence of tetraethylead in the neuroreflexory apparatus controlling ophthalmotonus. Changes on the part of the eye conform to the data of general pathology, thus determining the clinical picture of tetraethylead affection. It is characterised by the development of inhibiting process in central boundaries of nervous system.

Persons with pathological types of elastometric curves were investigated in inpatient department where the character of ophthalmotonus was determined by means of a dynamic method of its investigations by Maslennikov A. I.

Still in 1904–1905 Maslennikov was the first to propose to investigate ophthalmotonus in the morning and in the night. According to these investigations diurnal fluctuations of ophthalmotonus in healthy persons did not exceed 4.0 mm Hg.

While investigating persons dealing with tetraethylead a part of them revealed diurnal fluctuations to be increased dimensions of these fluctuations depending on the level of ophthalmotonus. This can be seen on the presented table.

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While investigating persons dealing with tetraethyllead a part of them revealed diurnal fluctuations to be increased, dimensions of these fluctuations depending on the level of ophthalmotonus. This can be seen on the presented table.

TABLE — *The level of Ophthalmotonus and its diurnal Fluctuations in mm Hg*

Level of Ophthalmotonus	No		Diurnal Fluctuations							
	Persons	Eyes	Norm to 4,0 mm	5 0	6,0	7,0	8 0	9 0	10,0	Hig her
36 0-40 and higher	16	32	3	—	4	4	3	4	2	17
31 0-35 0	46	92	14	12	20	12	10	11	4	9
29 0-30 0	26	52	29	4	11	4	2	—	2	—
27 0-28 0	20	40	28	6	5	—	1	—	—	—
to 27 0	22	44	2	2	1					

Increased ophthalmotonus caused increased dimensions of diurnal fluctuations, regular rhythm of these fluctuations being disturbed as well. The changing of the increase and decrease in ophthalmotonus was taking place irregularly at various diurnal time and unequal in both eyes. Such unbalanced state of ophthalmotonus was determined by the development of neurosis in the apparatus controlling ophthalmotonus, this being characteristic of the clinical picture of affection by tetraethylead as well.

Changes in the organ of vision conformed to other signs of affection by tetraethylead. In contradistinction to inorganic lead investigated persons revealed no impairment in peripheral blood as well as no increased lead contents in urine.

Changing in gastric juice acidity and in normal type of glycaemic curve were characteristic of them.

On the basis of electrocardiogram data changing in conductive cardiac system were determined that was clinically manifested by either bradycardia or by tachycardia combined with arrhythmia.

The data obtained on the part of general state of the body testify the changes in the organ of vision to be only partial manifestation of general affection of the body by tetraethylead.

Stated toxic glaucoma appeared to be only some addition to the clinical picture of general affection by tetraethylead. The data obtained confirmed once more the presence of close connection and dependence of the eye on the body as a whole.

Observations on animals were carried out to answer a number of questions concerning pathogenesis of toxic glaucoma. For this purpose a method of gradual and lasting intoxication of animals by tetraethylead was elaborated.

In the period of acute intoxication by tetraethylead some animals lost weight some revealed growing bald, permeability of vessels was sharply impaired extensive haemorrhages appeared convulsion attacks developed in which case ophthalmotonus control was sharply upset Its increased level before the attack changed after it by sharp fall, sometimes below the norm.

In case of chronic intoxication of animals by tetraethylead cholinesterase activity of blood serum decreased The character of ophthalmotonus control was determined by pathological changes of elastometric curves increased fluctuations of ophthalmotonus level, and its frequent increase above the stated norm In separate animals the upset in ophthalmotonus control was kept under observation at the length of 1-2 years, thus determining chronic character of affection

In contradistinction to healthy animals in rabbits subjected to tetraethylead effect under the influence of adrenaline atropine, and pilocarpine elastometric curves of pathological types were frequently noted fluctuations being increased and ophthalmotonus reaching high level

Provocative investigations by pressing on the eye ball with the weight of 50 0 gr also confirmed pathological character of ophthalmotonus apparatus in animals subjected to the effect of tetraethylead

With the help of nephelometric method by Francheschetti and Willand the increase in protein contents in aqueous humour of animals subjected to tetraethylead effect was stated to be increased Increased permeability of eye membranes was determined as well in compression tonometric investigations by Vurhaft M B when after pressing on the eye with 15 0 ophthalmotonus decreased considerably and segment volume of tonometric flattening of the cornea reached large dimensions Lasting period of hypotony supervening the compression of the eye pointed out to simultaneous decreased aqueous humour metabolism

Lasting hypertension in case of small segment volume of tonometric flattening of the cornea as well as small decrease in ophthalmotonus pointed out to tetraethylead to be able to inhibit the process of aqueous humour formation

Tetraethylead influence on the ophthalmotonus control and development of toxic glaucoma can be explained by such complicated character of its influence

One more stated form of glaucoma of known etiologic factors, the production of this disease on animal models the studying of a number of questions concerning the pathogenesis of its development can help to work out prophylactic measures for preventing the development of this disease

The studying of toxic glaucoma can be of great use for elucidating a number of questions concerning the pathogenesis of glaucoma being a basic disease resulting in blindness



# **SCLERAL RIGIDITY IN MANAGEMENT OF OPEN ANGLE GLAUCOMA PATIENTS WITH MYOPIA**

**With Special Reference to Chinese Scleral Rigidity**

**PEI-FEI LEE, M D**

The scleral rigidity in patients with high myopia is often reported to be somewhat lower than that of the normal eye. The determination of coefficient of scleral rigidity is therefore desirable in the evaluation of intra ocular pressure when suspicion of early glaucoma with high myopic condition has arisen. This fact and uncertainty in interpreting the myopic disc appearance and visual field abnormalities make the early diagnosis of glaucoma especially difficult. The importance of early recognition of glaucoma in management of high myopic has been repeatedly emphasized by other investigators 1-3, 6-9, 11-14.

The method of Friedenwald for clinical estimation of ocular rigidity by means of repeated paired tonometric readings has been reevaluated by Kronfeld and apparently has worked reasonably well and is useful for clinical purposes (4). It is true that the Goldmann applanation tonometer is superior than the Schiøtz impression tonometer in estimating scleral rigidity but the impression tonometer of Schiøtz is more convenient than the applanation tonometer, (6), (9) and the method of Friedenwald can be used for clinical purposes, when the applanation tonometer is not available.

It is the purpose of this study to determine how important the scleral rigidity is in the management of high myopic patients who may have early glaucoma, and to report the estimated value of coefficient of scleral rigidity in normal eyes among a Chinese population.

## **METHOD AND MATERIAL**

Friedenwald's method of estimating scleral rigidity by means of repeated paired tonometric readings has been used in this investigation. All measurements were made by the author with a certified Schiøtz tonometer of American manufacture, during the hours from 8:30 to 12:30 A.M. and 2:30 to 6:00 P.M. with the patient in recumbent

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A portion of this paper was presented before the Third Joint Meeting of the Ophthalmological Society of the Republic of China and the Section on Ophthalmology, Formosan Medical Association on Nov. 25, 1963, Taipei, Taiwan and published in the Chinese M. J. 9: 261 (Dec.) 1962.

position. Applications of the tonometer of two to three seconds' duration were made and the oscillations of the pointer were carefully observed. The whole or half scale units closest to the average position of the pointer during the application was recorded as the reading. The applications were made first to the left and then to the right eye first with the lower weight and then with the higher weight. Thus the sequence was Left 5 5 right 5 5, left 10, right 10, and so forth. Because most people are more sensitive about their right eye and the position of examiner is on the right hand side of the patient the left eye was measured first in this series. For the purpose of avoiding immediate cardiac reflex and thus reducing technical error the tonometer was always held covering the visual line of the examined eye for two to three seconds prior to applying the tonometer on cornea. Every patient received at least two pairs of measurements per clinic visit and most of them had two clinic visits. Data were then added together and divided by times of measurements as the actual value. Coefficient of scleral rigidity was expressed according to the tables of Moses and Becker (6).

Tonography was practiced according to the method of Grant and tracings were made on an Esterline Angus recording unit with improved model MC Electronic Tonometer (V Mueller & Co). Intraocular pressure and facility of outflow (C) were calculated from the 1955 Calibration of the Committee on Standardization of Tonometers (AAOO). Goniocopy was done with Koeppel's lens, Barkan illuminator and Haag Streit binocular handmicroscope. The tabular method of Moses and Becker (6) using the following formula for the correct C value in eyes with abnormal scleral rigidity was applied in this investigation.

$$C = \frac{0.0215 \Delta V_g + (E - 0.0215) \Delta V_c}{4E (P_{t_{av}} - P_0 - 1.25)}$$

in which

- C is the coefficient of facility of outflow (Cu mm./min / mm Hg)
- $\Delta V_g$  is the change in ocular volume
- E is the coefficient of scleral rigidity as determined clinically
- $\Delta V_c$  is the change in corneal indentation volume during tonography
- $P_{t_{av}}$  is the average of initial and final intraocular pressure during tonography
- $P_0$  is the intraocular pressure of the undisturbed eye as estimated from scleral rigidity measurements with the Schiotz tonometer

The tonometric measurements reported herein were made on 570 normal and myopic eyes and on 29 myopic eyes associated with primary open angle glaucoma selected from the Eye Clinic National

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The tonometric measurements reported herein were made on 570 normal and myopic eyes and on 29 myopic eyes associated with primary open angle glaucoma selected from the Eye Clinic, National

Taiwan University Hospital. The basis for selection was compliance with the requirements of

- 1 Having unilateral myopia
- 2 Of being myopic and having received cycloplegic refraction
- 3 Of having no specific ocular pathology nor refractive error
- 4 Of being well relaxed, cooperative during the measurements, and with no history of glaucoma, and
- 5 Myopic eyes associated with primary open angle glaucoma

For the convenience of comparison the myopia patients were divided into the following four groups

- 1 Mild myopia (less than  $-3$  D)
- 2 Moderate myopia ( $-3$  D to less than  $-6$  D)
- 3 High myopia ( $-6$  D to less than  $-10$  D) and
- 4 Excessive myopia ( $-10$  D and over) \*

## RESULTS

### 1. NORMAL EYE

A total of 570 emmetropic, myopic and unilateral myopic eyes were investigated and the findings are shown in the table below

TABLE I — Shows the average value of coefficient of scleral rigidity in normal and myopic eyes

Eye Condition	Number of Eyes	Average $F$ value
Normal	236	0.0205
Myopia mild	54	0.0212
moderate	81	0.0202
high	38	0.0194
excessive	100	0.0167
Unilateral myopia		
Mild normal	15	0.0209
myopic	15	0.0207
Excessive normal	15	0.0211
myopic	15	0.0123

### EMMETROPIC EYES

In 236 normal eyes, the mean value of coefficient of scleral rigidity ( $F$ ) was 0.0205. Elder the age, higher the  $F$  was noticed in this series

Correlation coefficient between age and  $E$  is highly significant ( $r = 0.22 > 0.181$  when  $\alpha = 0.01$ ) (Fig. 1—A and B)

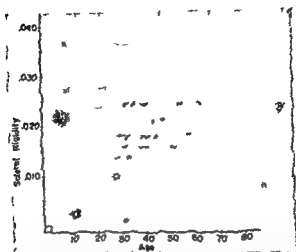


FIG. 1 A Relation of age to scleral rigidity. The frequency distribution of varying degree of scleral rigidity in 236 normal eyes is shown. Greater the value of rigidity the older the age of the patient. Most abnormally high rigidity was observed in the older age group.

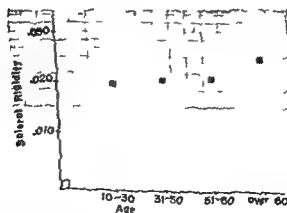


FIG. 1 B Relation of age to scleral rigidity in 30 normal eyes in each of the four age groups. Elder the age higher the rigidity is indicated. Correlation coefficient between age and  $E$  is highly significant ( $r = 0.22 > 0.181$  when  $\alpha = 0.01$ ).

## MYOPIC EYES

In 274 myopic eyes, the mean value of  $E$  varies according to the degree of myopia. Higher the myopia, lower the  $E$  was observed. It is also true in case of unilateral myopia (Fig 2—A and B). The differ

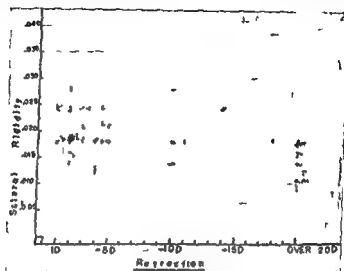


FIG 2 A Relation of myopia to scleral rigidity. The frequency distribution of varying degree of scleral rigidity in 274 myopic eyes. Lower than average normal value of rigidity is shown in the excessive myopia group.

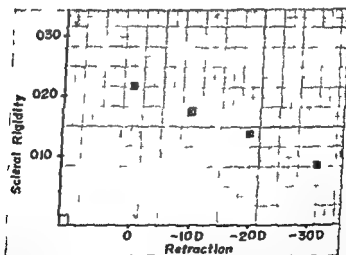


FIG 2 B Relation of scleral rigidity to axial refraction. This figure indicates the higher the degree of myopia the lower the average value of rigidity. Highly significant difference of the  $E$  value between 54 mild and 100 excessive myopia eyes is observed.

$$\left( \frac{M_1 - M_2}{\sqrt{m_1^2 + m_2^2}} = 3.2 > 3 \right)$$

ence of the  $E$  value between 236 normal and 54 mild myopia eyes was not significant but highly significant in normal and 100 excessive myopia eyes  $\left( \frac{M_1 - M_2}{\sqrt{m_1^2 + m_2^2}} = 4.7 > 3 \right)$  and also in 54 mild and 100 excessive myopia eyes  $\left( \frac{M_1 - M_2}{\sqrt{m_1^2 + m_2^2}} = 3.2 > 3 \right)$

For mild unilateral myopic cases, the mean of the differences of the  $E$  values between 15 normal and mild myopic eyes (Difference =  $E$  value of normal eye - myopia) has a 95% confidence interval of 0.0039 - 0.019. For 15 normal and excessive myopic eyes the corresponding mean has a 99% confidence interval of 0.0108 - 0.0026. Therefore, for excessive unilateral myopia cases, it can be concluded that the normal has higher rigidity than the myopic eye, but for the mild unilateral myopic cases the same conclusion cannot be drawn.

#### TONOGRAPHIC AND GONIOSCOPIC FINDINGS

1 Excessive myopia Eleven of sixty excessive myopia cases received tonography and gonioscopic examination. Two of these eleven cases showed slightly low outflow facility. However, this poor outflow facility apparently was due to the low  $E$  value rather than pathologically increased outflow resistance. These  $C$  values were well within normal range after scleral rigidity correction (Fig. 3 - A and B). Chamber angles were wide open and with no pathological finding gonioscopically in this group.

2 Unilateral myopia Tonography and gonioscopy were performed in five of the 10 cases with unilateral mild myopia and 15 with unilateral excessive myopia. The contralateral eye was normal and



FIG. 3 A Tonography tracings from an unilateral excessive myopia patient. Upper curve shows decline in myopia eye, lower curve shows a normal  $C$  value in contralateral (normal) eye.  $E$  and  $P_0$  corrections are also indicated.



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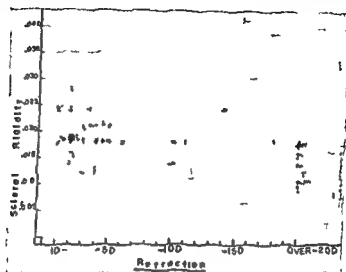


FIG 2 A Relation of myopia to scleral rigidity. The frequency distribution of varying degree of scleral rigidity in 274 myopic eyes. Lower than average normal value of rigidity is shown in the excessive myopia group.

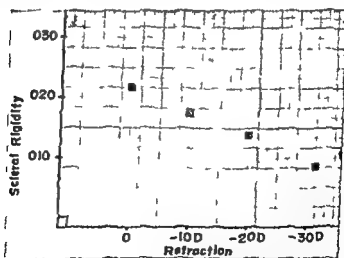


FIG 2 B Relation of scleral rigidity to axial refraction. This figure indicates the higher the degree of myopia the lower the average value of rigidity. Highly significant difference of the  $F$  value between 54 mild and 100 excessive myopia eyes is observed.

$$\left( \frac{M_1 - M_2}{\sqrt{m_1^2 + m_2^2}} = 3.2 > 3 \right)$$

TABLE II — Coefficient of scleral rigidity in 15 unilateral excessive myopics

Case No	Age	Sex	Tonomet Reading (R)		C — Value				Ref Index
			Eyes	R5 5/R10 0 Gm	E	Po corr	Before E Correc tion	After E Correc tion	
1	33	F	OD OS	5 25/ 9 5 6 25/11 75	0 0294 0 0139	13 5 19	0 24 0 20		Em —22 D
2	53	F	OD OS	6 /11 75 5 / 9 25	0 0163 0 0294	15 5 14	0 27 0 30		—23 D Em
3	11	M	OD OS	8 /14 5 7 /12 75	0 0087 0 0124	18 17	0 26 0 27		—20 D Em
4	57	F	OD OS	4 5/11 4 5/9 5	0 0076 0 0180	27 21	0 10 0 22	0 28	—25 D Em
5	26	F	OD OS	5 /11 4 5/8 75	0 0104 0 0795	24 16	0 20 0 26	0 30	—12 D Em
6	63	F	OD OS	5 5/10 5 6 25/13	0 0182 0 0096	18 20 5	0 19 0 11	0 22	Em —18 D
7	37	F	OD OS	4 /9 4 /9	0 0172 0 0172	22 22	0 11* 0 27		—20 D Em
8	42	F	OD OS	6 /11 5 4 5/9	0 0128 0 0180	20 21	0 26 0 26		—17 D Em
9	61	M	OD OS	6 /12 4 5/9 5	0 0107 0 0713	21 18 5	0 31 0 29		—25 D Em
10	47	M	OD OS	7 /12 5 9 /15 5	0 0139 0 0098	16 15	0 23 0 70		Em —16 D
11	41	M	OD OS	5 /10 6 /12	0 0182 0 0107	19 21	0 32 0 23		Em —12 D
12	49	F	OD OS	7 /11 5 7 25/14	0 0237 0 0078	11 20	0 26 0 21		Em —16 D
13	29	M	OD OS	6 5/12 5 7 5/14	0 0109 0 0086	19 19	0 22 0 14	0 19	Em. —11 D
14	53	M	OD OS	7 /12 6 /10 5	0 0179 0 0243	14 13	0 23 0 27		—12 D Em
15	18	F	OD OS	6 5 12 5 75/11	0 0139 0 0159	17 18	0 24 0 26		—10 D Em
Average			Em. Myopia	5 47/10 40 6 37/12 33	0 0211 0 0129	17 13 19 53	0 257 0 204		Em —17 25 D

\* Borderline diurnal variation in IOP and positive water drinking test were also observed in this case.

Correction for C — value was made only in eyes which were more suspicious

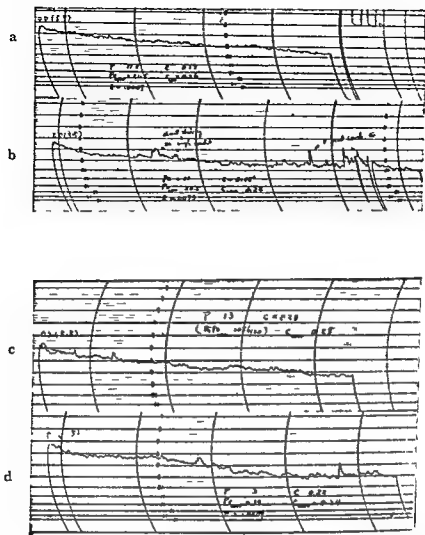


FIG 3B Tonography tracings from a bilateral excessive myopia patient who received the therapeutic pilocarpine test in OD. Control eye OS. Upper curves (a,b) show apparently low  $C$  value OU especially in OD prior to pilocarpine test. Lower curves (c,d) showed  $C$  value  $P_0$  and  $F$  were essentially unaffected by pilocarpine medication in OD. There is essentially no change in control eye  $C$  value and  $P_0$  corrections also indicated.

with no refractive error in all cases. Outflow facility appeared low in four of 15 excessive myopic eyes, but outflow facility in three of these four cases was well within the normal range after  $F$  correction. Early open angle glaucoma was suspected in the remaining one case. The  $F$  value of the two eyes was identical in this individual (Case 7) (Table II).

Chamber angles were wide open in all cases of unilateral myopia and showed no angle pathology gonioscopically.

Case No.	Age	Sex	F			T			E	J	Inf L Co ct	Inf F Correct
			Prs	R5	5 R10 0	R5	5 R10 0					
1	60	M	OOD	6	0 1 9	0107	21	0 07	0 11			
2	51	M	OOD	3	0 10 5	0088	31	0 03	0 09			
3	38	M	OOD	4	5 10 5	0199	9	0 14				
4	25	M	OOD	4	5 10	0197	32	0 08				
5	35	M	OOD	2	5 7 5	0238	26	0 10				
6	24	M	OOD	2	5 9 5	0217	19	0 15				
7	32	M	OOD	3	0 8	0175	6	0 11				
8	21	F	OOD	2	0 8 5	0166	44	0 12				
9	13	M	OOD	2	0 9 5	0246	16	0 10				
10	59	M	OOD	5	0 9 5	0180	21	0 07	0 07			
11	46	M	OOD	4	5 9 5	0182	19	0 05	0 14			
12	37	M	OOD	3	5 9 5	0194	34	0 06	0 14			
13	51	M	OOD	2	5 7 5	0247	27	0 05	0 14			
14	43	F	OOD	3	5 8 5	0183	41	0 12	0 14			
15	20	M	OOD	2	5 10	0182	19	0 10	0 14			
16			OOD	5	0 10	0182	19	0 11	0 14			
17			OOD	5	0 11 5	0080	25	0 06	0 14			
18			OOD	6	0 11 5	0139	19	0 16	0 14			
19			OOD	4	0 9	0177	22	0 11	0 14			
20			OOD	4	0 9	0172	22	0 27	0 14			
21			OOD	3	0 8 25	0173	26	0 10	0 14			
22			OOD	2	5 7 25	0203	27	0 08	0 14			
23			OOD	2	5 7	0238	26	0 10	0 14			
24			OOD	2	5 7	0231	28	0 13	0 14			
25			OOD	2	0 6 5	010	11	0 04	0 14			
26			OOD	2	5 9 5	0155	32	0 07	0 10			
27			OOD	4	5 11			0 07	0 10			

... which were more numerous

Correction for  $C_{\infty}$  value as made only in eyes which were more than 1000  $\mu$ m from the nearest incision prior to operation

• Post ridgeotomy and cautery OU but myopic was present prior to operation

1981] = Glaucoma existed for three years before the ophthalmologist realized the

visual and field loss were observed at the time when glaucoma was recognized.

C2 = Early cure of the opt c d sc OD and normal OS Further investigation

Lately, coupling of the optical axis of the objective lens and the optical axis of the eyepiece lens was accomplished by means of a micrometer lens.

+Tone meter reading with 7.5 and 15 Gm weights

marked cupping and atrophy of the optic disc associated with

## INCIDENCE OF GLAUCOMA

It is interesting to note that two early cases and one suspected case of open angle glaucoma were observed in the myopia group, three established and two suspected early open angle glaucomas were found in the normal eye group incidentally. All of these eight cases were not included in the 570 eyes mentioned above. Incidence of glaucoma was 1.08% and 1.24% respectively.

Myopia with glaucoma. Among four early open angle glaucoma (including one suspected) cases in the myopia group, two were excessive, and two were mild myopes.

## II GLAUCOMATOUS EYE

A group of 16 myopic patients (29 eyes) associated with primary open angle glaucoma were investigated and the findings are shown in Table III on page 1297.

## COMMENT

Coefficient of scleral rigidity ( $E$ ) varies not only in a variety of ocular diseases but also in subjects with normal eyes. Therefore to determine the scleral rigidity is essential in the evaluation of intraocular pressure. The average coefficient of scleral rigidity in normal eyes has been reported as 0.0215 (Friedenwald and Kronfeld), 0.0217 (Drance) and 0.0204 (Kishimoto et al). The difference between 0.0215 and 0.0204 is statistically not significant (Kishimoto et al) <sup>(7)</sup>. The average coefficient of scleral rigidity in normal eyes among Chinese was 0.0205 and is in agreement with Kishimoto et al and Friedenwald. Therefore, the 1955 Calibration (AAO) would be equally acceptable to a Chinese population.

Friedenwald has investigated the coefficient of scleral rigidity in normal eyes in four age groups: 15-30, 31-50, over 50 and over 60 years respectively. The greater value of  $E$  was observed in the older group. He also stated it is evident that an increasing rigidity of the ocular coats was characteristic of advancing age. This change is first perceptible in the fifth decade, and it is certainly not uniform for all individuals, since even among persons of over 80 years a considerable number are found whose ocular rigidity is not greater than that of the average young normal adult <sup>(11)</sup>. Drance investigated ocular rigidity in 1,011 normal eyes with applanation tonometer and stated that  $E = 0.0217$  and found no relationship to age <sup>(10)</sup>. Kishimoto et al <sup>(7)</sup> stated that scleral rigidity showed no relation to age in 216 normal eyes. Schneider et al <sup>(9)</sup> reported that there does not appear to be an appreciable increase in  $E$  in aged patients. Unfortunately they have investigated only suspected glaucoma patients, not normal eyes. Therefore their data could not be considered of much use in evaluation of coefficient of scleral rigidity in normal eyes.

The coefficient of scleral rigidity of the normal eyes in the present series showed a highly significant tendency to increase with age. The frequency of age distribution of varying degrees of rigidity and the

cases showed lower scleral rigidity. However, the outflow facility in those three patients (5 eyes) was remaining impaired after scleral rigidity correction (cases 1, 12 and 16 Table III). It is obvious that the data of excessively myopic eyes with glaucoma investigated in this series would have been more agreeable had this segment case been available for investigation.

Grant<sup>(15)</sup> has advocated that the use of the  $Po/C$  ratio for differentiating glaucomatous and non glaucomatous eyes, with the dividing line about 100 when using the 1955 calibration. Using the uncorrected value for  $Po$  and the uncorrected value for  $C$  the ratio comes out about the same as when both values are corrected for abnormalities of scleral rigidity. According to his suggestion I have plotted the excessively myopic, both glaucomatous and non glaucomatous eyes with lower scleral rigidity (Table 2 and 3) and all of the myopic eyes with glaucoma (Table 3) into the diagrams below which are in agreement with and further supported Grant's work (Graphs 1 and 2).

The advantages of the  $Po/C$  ratio for differentiating glaucomatous and non glaucomatous eyes are simple, convenient and helpful in management of myopic patient at daily office practice.

It is often emphasized that the myopic eye represents a special problem in the management of glaucoma. Many myopic eyes have gone blind from primary or secondary glaucoma without the patient or ophthalmologist being aware of the existence of glaucoma.

This statement was apparently true in cases 1 and 12 of the table III. The reason for this difficulty are (1) the distance between level of lamina cribrosa and retina in myopic eyes is much less than in normal or hyperopic eyes. (2)  $C$  value is usually somewhat lower in myopic eyes than in normal eyes and (3) visual field abnormalities are induced by the large conus and choroidal atrophy in myopes. Furthermore to interpret the appearance of the disc in high myopia is more difficult than in normal eyes if myopic cupping and large conus are present. Many of these discs look atrophic and the myopic conus may add to the confusion. However, I would agree with Goldmann's opinion that glaucomatous cupping in myopic eyes usually begins or is detectable at the nasal side of the optic disc and may be associated with displacement of vessels.<sup>(12)</sup> Chandler has often said that the way to detect early cupping is to take a good look with the ophthalmoscope not just a brief or quick examination.<sup>(14)</sup> Therefore careful fundoscopic investigation of the optic disc and the influence on ocular tension and  $C$  value if kept in mind should be adequate in handling myopic patients with or without glaucoma. It may be emphasized that (1) in management of excessive myopia the possibility of early glaucoma should be kept in mind especially in elder individuals and (2) in evaluation of ocular tension in myopia the scleral rigidity influence should be considered especially in case of myopic cupping. However the glaucoma incidence is not greater in excessive myopia than in normal eyes.

rigidity distribution curve for different age groups in normal eyes are shown in Figure 1 — *A* and *B*. This finding is in agreement with Friedenwald's work but not with the other.<sup>17, 18)</sup>

It has been reported that scleral rigidity in high myopia (more than — 10 D) is lower than that of normal eyes.<sup>11, 12, 13, 14, 27)</sup> Myopic eyes were investigated in this series and the findings are in agreement.<sup>11, 12, 13, 14)</sup> The higher the degree of myopia, the lower the *E* value was observed (statistically, the difference of mean of *E* value is highly significant) (Fig 2 — *A* and *B*). Diaz Domingue<sup>25)</sup> investigated the relationship of glaucoma and high myopia. He performed tonography in 25 of 100 patients with high myopia and ocular tension below 21 mm Hg. Of the 25 patients only eleven had normal outflow facility. According to Bock and Stepanik<sup>26)</sup> in 57 excessive myopic eyes with suspected glaucoma, diagnosis was established in 35 with the help of tonography. This fact would make one wonder whether the glaucoma incidence really is that high (more than 50%) in high myopia. If so, a large per cent of high myopic eyes would have lost their sight or become blinded over a period of years. However, clinically we have not observed this condition nor the incidence of glaucoma is any higher than that of normal eyes. Two of eleven tonographed excessively myopic eyes (Over 10 D) showed decrease in outflow facility in this series and were found to be well within normal range after scleral rigidity correction and showed no other evidence of glaucoma during the past two year follow up. Therefore, one would assume that many of the high myopes in reports mentioned above would turn out to have normal outflow facility if the scleral rigidity correction was made as Moses and Becker have suggested.<sup>16)</sup>

For further comparison a number of unilateral myopes were investigated. Coefficients of outflow facility were found low in four of 15 excessively myopic eyes but not low in 15 mild myopes. Of four seeming to have decreased outflow facility, three were actually normal after scleral rigidity correction and one showed borderline diurnal variation of ocular tension and drinking test in addition to the impairment of outflow facility after the scleral rigidity correction. Therefore early open angle glaucoma was suspected (or established) in this case (Table II, case 7).

A total of 26 excessive myopes (11 bilateral 15 unilateral) have received tonography and six of these cases showed low outflow facility but five actually had a normal outflow facility after the scleral rigidity correction. In one case early open angle glaucoma was established. The cases of excessive myopia existed for years and have demonstrated no significant evidence of glaucoma. This fact well demonstrated that outflow facility with uncorrected scleral rigidity in eyes with excessive myopia would offer little of value in the early diagnosis of glaucoma and may be even dangerous if one would use this kind of outflow facility as an important diagnostic criterion or sole guide in determination of necessity for operation.

A group of 16 myopic patients (29 eyes) with primary open angle glaucoma were received routine glaucoma work up and three of these

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A group of 16 myopic patients (29 eyes) with primary open angle glaucoma were received routine glaucoma work up and three of these

## SUMMARY

The Coefficient of scleral rigidity in 570 normal bilateral myopic and unilateral myopic and in 29 myopic with primary open angle glaucoma eyes was evaluated by the method of Friedenwald using only the schiotz tonometer and comparing readings with 2 weights.

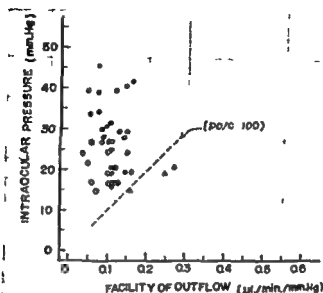
In normal eyes the mean value of coefficient of scleral rigidity was found to be higher in the elder age group. There is no significant difference of mean value of coefficient of scleral rigidity between Chinese and Westerners. A lower the coefficient of scleral rigidity was observed in excessive myopia but no significant difference was found between normal eyes and those with mild myopia. It is also true in myopia eyes with primary open angle glaucoma.

It is suggested that in management of excessively myopic patients the possibility of abnormal scleral rigidity and its influence on apparent intraocular pressure and outflow facility should be kept in mind.

Using the Po/C ratio with the dividing line about 100 for differentiating glaucomatous and non glaucomatous myopic eyes as advocated by Grant are convenience and helpful in daily office practice.

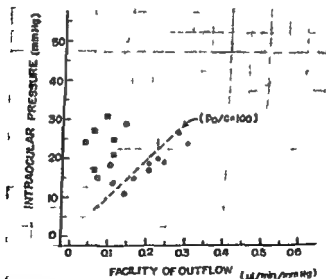
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GRAPH 1 Twenty seven glaucomatous eyes with myopia and two non glaucomatous eyes with myopia were plotted with Grant's diagram  $P_o/C = 100$  dividing line to differentiating glaucomatous and non glaucomatous eyes

Open circle = uncorrected  $P_o$  and  $C$  closed circle = corrected  $P_o$  and  $C$  in glaucomatous eyes Open triangle = uncorrected  $P_o$  and  $C$  closed triangle = corrected  $P_o$  and  $C$  in non glaucomatous eyes



GRAPH 2 Three glaucomatous eyes with excessive myopia and five non glaucomatous eyes with excessive myopia were plotted as in graph 1

Open square = uncorrected  $P_o$  and  $C$  closed square = corrected  $P_o$  and  $C$  in glaucomatous eyes Open circle = uncorrected  $P_o$  and  $C$  closed circle = corrected  $P_o$  and  $C$  in non glaucomatous eyes

It is interesting to note that this new technique was evolved as a result of the author's observing four cyclodiathermy dialysis patients develop an acute attack of glaucoma from pupillary block.

# TECHNIQUE

A drop of pontocaine 0.5% is instilled into the conjunctival sac every four minutes for four times. Following the usual face preparation anesthesia is obtained by Van Lint's method, together with retrobulbar injection of 2 cc. of 2% xylocaine through the skin at the inferotemporal margin of the orbit.

A lid speculum is put into place, and the superior rectus suture is inserted. The conjunctiva and Tenon's capsule are incised 5 mm. from the limbus, the incision extending either from 11 o'clock to 3 o'clock position or from 1 o'clock position to 9 o'clock. Both layers are carefully separated from the sclera with Steven's scissors extending forward to the limbus. The posterior lip of the conjunctival incision is dissected from the sclera to as far back as 2 to 3 mm., avoiding the area of the superior rectus muscle. The flap of Tenon's capsule and conjunctiva is then reflected using a 6-0 black silk suture. All persistent bleeders are mildly cauterized to prevent blood from trickling into the anterior chamber later.

With a Bard Parker No. 15 blade a scratch incision about 4 mm. in length and 0.5 mm. in depth is made perpendicular to the surface of the sclera and 6 mm. from the limbus. Then two rows of partial penetrating diathermy applications, two on each side arranged in a V-shaped fashion, are made, utilizing a 1 mm. pin electrode and 35 milliamperes of current (Walker Unit). Currently, the author uses a four-pinned electrode prepared by Storz Co. The length of application of electrode should not exceed 3 to 4 seconds.

Then a single armed 6-0 black silk suture is inserted 4 mm. behind the posterior lip of the conjunctival incision, through the posterior lip of the scleral scratch incision, then looped and through the anterior lip of the scleral incision. Finally this suture is continued through the posterior lip of the conjunctival incision 1 mm. in front of the insertion of the other end of the suture. At this stage of the surgery the scratch incision is made deeper until its midsection reaches the darkish outer border of the ciliary body. A trial insertion of the cyclodialysis spatula is then made to verify whether or not the line of cleavage between the sclera and ciliary body has already been established (no actual cyclodialysis yet).

Then at the 12 o'clock position an ab externo scratch incision is made perpendicular to the scleral surface 1 mm. behind the limbus. After a 6-0 black silk suture has been preplaced as in the aforementioned scleral scratch incision, the ab externo incision is deepened until the chamber has been entered. This stage is usually ushered in by a tiny iris prolapse. If no iris tissue presents, gentle pressure should be applied 1 mm. above the ab externo incision.

## CYCLODIATHERMY-DIALYSIS IRIDECTOMY

### A Preliminary Report of One-Hundred nine Eyes Undergoing This Operation

ULYSSES M. CARBAJAL, M.D.,  
*Manila, Philippines*

This paper presents a combination method for performing a filtration operation for angle closure glaucoma that has lasted more than 36 hours as well as for chronic simple glaucoma, especially when the angle tends to be narrow. It is a modification of cyclodiatrermic dialysis, a method advocated by the author <sup>(1)</sup> for glaucoma patients, particularly those with contracted visual fields and definitely diminished outflow facility. A "tunnel" is produced connecting the anterior chamber and the suprachoroidal space by multiple thrust cyclodialysis and by cyclodiatrermic applications along the border of the proposed "tunnel." In addition to this, a peripheral iridectomy is performed through an ab externo incision at 12 o'clock position before the cyclodiatrermic dialysis is completed on the upper outer or upper inner quadrant.

The combination of iridectomy and cyclodialysis is not altogether new, having been suggested by Czermak <sup>(2)</sup> in 1906. Other advocates of this, although in various modifications, were Ruber <sup>(3)</sup>, Queiroga <sup>(4)</sup>, Wootton <sup>(5)</sup>, Wheeler <sup>(6)</sup>, Goldmann <sup>(7)</sup>, Allen <sup>(8)</sup>, and Posner <sup>(9)</sup>.

Although the rationale for combining iridectomy and cyclodialysis has not been completely clear, the following points have been considered: (1) When combined with cyclodialysis, the peripheral iridectomy tends to deepen the anterior chamber, thereby enhancing permanence of the internal fistula. (2) Since a shunt is made between the anterior and posterior chambers, pupillary block is prevented. (3) There may be improvement of filtration through the trabecular spaces that may occasionally be torn open by the cyclodialysis and possibly by the iridectomy if basal enough.

In the new operation herein described the author adds cyclodiatrermic to the already well known cyclodialysis iridectomy combination, which is done through separate incisions. The rationale for the diathermy along the proposed "tunnel" is to promote "pillar formation" that will not only prevent hypotony but also lessen the chances for complete reattachment of the ciliary body to the sclera. Moreover, the diathermy application diminishes the danger of surgical hyphema. The subsequent ciliary body atrophy is not of much significance, as the area covered by the diathermy is approximately 1/16th of the entire ciliary body area.

The following criteria were used in evaluating results obtained from this procedure: (1) Tension was normalized — not higher than 25 and not lower than 7 mm Hg Schiotz; (2) Vision was preserved or improved; (3) Visual fields were maintained or improved; (4) Aqueous outflow facility was increased; (5) A cleft or tunnel entrance, however small, was demonstrable by gonioscopy; (6) The patient himself was satisfied over the result — headaches gone, eye not disfigured, no need for diamox and the like.<sup>1</sup>

The results in controlling tension have been quite gratifying. Except in five patients the pressure was normal two months or longer after operation. The average intraocular pressure reading was 42 mm Hg Schiotz before surgery, this dropped to 15 (average) after surgery. The incidence of hypotony was only 2, but this was only temporary.

Vision was preserved in all patients although in the first two weeks following surgery a few had blurry vision resulting from transient astigmatism. It is noteworthy that the three patients with just light perception before surgery did not lose this ability, but rather picked up in light perception field, the vision improving to CF in one. In the two hypotony cases vision improved to 20/40 as the pressure came back to normal.

In the great majority of the cases, the visual fields expanded concentrically or segmentally by 5 to as much as 15 degrees, and in patients with only glaucoma the blindspots stopped enlarging or became almost normal in size again. This was observed especially in those patients in which the pressure was brought down to 8–12 mm Hg Schiotz. This finding is in accord with that of L. Gross.<sup>2</sup> However, after the lapse of 2 to 3 years following surgery, a few showed some visual field loss.

Excepting six all eyes undergoing tonography both preoperatively and postoperatively showed some improvement in the facility of outflow. Gonioscopy revealed the presence of a cleft of varying sizes in all these eyes. It should be concluded, however, that facility of outflow is directly related not to the apparent size of the cleft but rather to the actual area of drainage which is extremely difficult to evaluate even gonioscopically or biomicroscopically.

Patients that found no relief from medications (drops, ointment, pills) were very grateful for the feeling of well being obtained after the surgery and for the diminution or even discontinuance of medications. Three patients diagnosed by general practitioners to be suffering from labyrinthitis proved the most grateful of all the patients undergoing this procedure.

# COMPLICATIONS

Complications were never serious except in one case of rubeosis iridis in which glaucoma recurred two weeks after surgery due to persistent and repeated postoperative hyphema. Primary hyphema

The iris root is carefully grasped for peripheral iridectomy avoiding too much loss of aqueous. The iris is gently repositioned in a milking fashion, until the pupil becomes roundish again. The limbal preplaced suture is now tied over the conjunctival flap. If considerable aqueous has been lost, normal saline or air should be injected to reform the chamber. This will prevent lens injury and undue hyphema when cyclodialysis is subsequently done.

Then cyclodialysis is carried out by inserting the cyclodialysis spatula gently and by following the line of cleavage until the scleral spur is passed and the spatula tip is barely seen in the periphery of the anterior chamber. Steady fixation of the anterior lip of the scleral incision should be done while the spatula is being pushed along and is hugging the inner scleral surface. Without withdrawing the spatula completely, seven to nine thrusts are made in an overlapping fashion, usually aiming at the 12 o'clock position and then working towards the 3 or 9 o'clock positions, depending on which quadrant and which eye is being operated on. It is important to avoid making thrusts directly in front of the tendon insertions in order to spare the ciliary vessels from damage. If the thrusts have been done correctly, there is no need for sweeping the spatula side to side, as they may rip some branch vessels open.

The scleral incision is then closed by cautiously pulling the ends of the preplaced suture and tying a square knot snugly. The incision in the conjunctiva and Tenon's capsule is closed by continuous 6-0 black silk suture. Neosporin and pilocarpine ointments are instilled. Both eyes are patched to promote ocular rest and thus prevent postoperative hyphema.

#### PRESENTATION OF DATA

The operation was performed upon 109 eyes of 79 patients, 35 of whom were females. Racial distribution was as follows: Caucasian — 35, Negro — 16, Mexican — 9, Filipino — 18, Japanese — 1. As to type of glaucoma, there were 103 eyes falling under the category of PRIMARY, and only 6 eyes under SECONDARY. Of the PRIMARY, 83 were chronic simple, 15 angle closure, and 5 absolute. Of the SECONDARY, 2 eyes had developed acute glaucoma from eye injury, 1 from rubeosis iridis, 1 following cataract extraction in which no iridectomy was performed, and 2 from unknown causes.

As much as possible, glaucoma work up was done in all the patients before and after glaucoma surgery. This consisted of (1) thorough history and careful physical examination, (2) visual acuity tests, (3) funduscopy, with emphasis on cupping of the nerve head and the status of the retinal vessels, (4) repeated tonometry, (5) visual field investigation with small and large targets, (6) slit lamp examination to determine depth of chamber and status of the lens, (7) gonioscopy, and (8) tonography. Provocative tests were resorted to only in borderline cases.

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(very slight) occurred during operation in about one fourth of the 109 eyes undergoing surgery, while secondary hyphema was seen on the second or third postoperative day in 5 eyes. In all the eyes with slight hyphema during surgery, the anterior chamber cleared completely, or almost so, on the first postoperative day.

Another complication that required close attention was uveal reaction during the first few days after surgery. This required topical and/or systemic steroids. In two eyes with moderate uveal reaction leading to transient posterior synechiae, spotty cortical lens opacities were also observed. No malignant glaucoma, no sympathetic ophthalmitis, and no eye infection occurred.<sup>1</sup>

### INDICATIONS AND CONTRAINDICATIONS

Cyclodiathermy dialysis iridectomy surgery is ideal for patients with an acute attack of glaucoma (angle closure) that has persisted over 36 hours. It is ideal for chronic simple glaucoma with rather narrow angle, or where there is a threat of peripheral anterior synechia formation. Secondary glaucoma resulting from blockage in the angle by synechiae or inflammatory deposits may be controlled by this type of surgery. In absolute glaucoma, in which the presence of an intraocular tumor has been ruled out, this procedure might save the eye from enucleation.

On the other hand, this procedure is contraindicated in rubeosis iridis regardless of etiology, and in eyes with cataracts. It is extremely dangerous to perform the peripheral iridectomy portion of this procedure in cases of aphakia in which no iridectomy had been previously done.

### MERITS OF THE OPERATION

*The operation is simple and safe, and can be finished in 15 to 20 minutes. Since the pupillary sphincter is preserved and since no iris pillar is incarcerated the cosmetic appearance is quite satisfactory and annoying glare and foreign body sensation from big blebs are avoided. The incidence of hypotony, malignant glaucoma, sympathetic ophthalmitis, and eye infection is definitely less than in other glaucoma operations. This procedure may be done either in the nasal or temporal quadrant.*

### SUMMARY

A modified glaucoma operation consisting of cyclodiathermy cyclodialysis and peripheral iridectomy is described. Indications, contraindications, complications, and merits of the operation are enumerated and discussed. Thus far the procedure has been quite effective in controlling ocular tension in 18 of 79 glaucoma patients. The operation, however, cannot be evaluated fully until more time has elapsed and other surgeons have had an opportunity to report their own results.

We found out that the basic condition securing the successful result of the operation is the close fitting of the transplanted mucosa flaps to the sclera. We achieved this fixing the mucosa flaps to the sclera by means of episcleral sutures instead of sewing them to the conjunctiva or rectus muscles as it had been performed formerly. Such fixing provides good healing of the transplanted flaps to the sclera.

In many cases it is sufficient to perform only the first operation of removing symblepharons to eliminate both partial and extensive adhesions of one and sometimes even of two eyelids.

This operation results in the restoration of the fornices, the correct position of the eyelids and a good closing of the rima palpebrae.

If the operation has been performed owing to total symblepharon of both the eyelids, then soon after the operation there takes place a scar shrinking of the mucosa transplanted on the wound surface of the eyelids and as a result an entropion and lagophthalmos reaching sometimes 10-12 mm develops.

The inability to close eyelids brings on the drying out of the operated eye. The patient feels the deterioration in the state of his eye after the operation.

We worked out the second operation — the second stage of removing the symblepharon performed three weeks later after the first one. This operation permits to remove completely this grave state. It consists in separation of the scar shortened mucosa, its elongation by means of a piece of the buccal mucosa which is common for both lids and blepharorraphy, no shrinking of the transplanted flap takes place as there is one piece of the mucosa and blepharorraphy. Three four months later when the process of scarring are already over the lids are incised along the line of their suturing.

The stages of surgical treatment described here vary depending upon the gravity of the injury and permit us to operate successfully even the gravest forms of symblepharons which up to now were considered incurable.

In this report we dwell upon the results of treating 500 patients who had 555 eyes operated. 222 patients (44.4%) were under our observation from 1 to 10 years, 52 (10.4%) — from 6 to 12 months and 176 (35.2%) — less than 6 months. Prolonged observations over more than the half of the operated patients give the possibility to draw final conclusions on the efficiency of our method of surgical treatment of extensive and total symblepharons. The operated patients were mainly of younger age group: 331 (66.2%) patients were at the age from 20 to 40, 73 (14.6%) — from 10 to 20 years old.

The character of eye injury was very serious. 219 patients (43.8%) had both the eyes injured. 249 patients (49.8%) had been unsuccessfully operated in other ophthalmological institutions. Only on 99 eyes (17.8%) out of 555 operated ones there was a partial symblepharon (i.e. either one or two eyelids). On 163 eyes (29.4%) there was either an

## EFFICIENCY OF OUR METHOD OF TREATING GRAVE CONSEQUENCES OF EYE BURNS

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In the Soviet Union extensive work is carried out on safety and protection of health of people working in plants where eye burns may occur owing to special kind of work. Nevertheless accidents still take place. Sometimes eye burns result in deep changes, leading to deterioration of vision and even blindness. The loss of vision in the majority of such cases is due to the adhesions of the lids with the eye globe and the development of leucomas. Changes in the posterior section of the eye occur less frequently, mainly after chemical burns with ammonium, lime, soda and some other chemicals.

Thus, ophthalmologists have to deal mainly with symblepharons, and leucomas in patients with consequences of eye burns.

In principle there is the possibility of restoring or improving the vision in such patients after removing symblepharons and leucomas.

However, up till now it was a very serious problem as there was no effective method of removing extensive and total symblepharons.

In books on eye surgery as well as in articles of separate authors there is no effective method of removing symblepharons of different gravity (A. Elschning, 1922, V. P. Odintsov and K. H. Orlov, 1933, H. Thiel, 1945, A. A. Colen, 1950, Arruga, 1953, A. Callahan, 1955, A. F. Rumyantseva, 1956, H. B. Strillard, 1958 etc.).

We worked out the method of surgical treatment of extensive and total symblepharons which gave favourable results (N. S. Pouchkovskaja, 1951, 1954, 1955, 1960).

The efficiency of this method was confirmed by G. V. Iegheza (1955-56).

At present we possess extensive clinical data in this direction. Over 500 patients with grave consequences of eye burns were operated after this method in the Filatov Institute; now we may draw definite conclusions on the efficiency of this method. I shall dwell upon the main principles of our method which consists of one or two operations depending on the extension of symblepharon. In the first operation incision of the adhesions and transplantation of mucous membrane separately on the wounded surface of the sclera and on the wounded surface of the lids is effected.

TABLE 1 — Results of Surgical Treatment Depending on Initial State of Operated Eyes

Initial State of Operated Eyes	Number of Eyes	Results of Treatment Number of Eyes	
		Success	Failure
Partial symblepharon of one or both eyelids	99	99	—
Extensive symblepharon of one eyelid	115	111	4
Extensive symblepharon of both eyelids	145	140	5
Total symblepharon of one eyelid	48	48	—
Total symblepharon of both eyelids	109	99	10
Total symblepharon and ankyloblepharon of both eyelids	39	36	3
Total	555	533 (96%)	22 (4%)

after burns. Here are some data out of the case histories of the patients operated by us.

Patient P 22 years old case hist Nos 35810 38577 Burn of the left eye with soda two years ago. Extensive symblepharon of both the eyelids overgrowth of scar tissue on the cornea vascularized leucoma of the left eye visual acuity equals to correct light projection (Fig 1). The right eye is healthy. At first the symblepharon was removed on



FIG 1 Patient 1 Extensive symblepharon of both the eyelids overgrowth of scar tissue on the cornea vascularized leucoma of the left eye

extensive or total symblepharon of one eyelid, on 25 eyes (45.8%) there was either an extensive or total symblepharon of both the eyelids and on 39 eyes (7%) there were total symblepharons and ankyloblepharons of both eyelids

On all the eyes there were total or partial vascularized leucomas, in many cases there was the overgrowth of scar tissue on the corner

Burns with lime occupied the first place — 163 patients (32.6%), then there were burns with melted metal — 96 patients (19.2%), with alkali — 84 patients (16.8%) and other substances — 50 patients (10%)

The gravity of the initial state is evident from the visual acuity of the operated eyes that equalled

wrong light projection	on 212 eyes,
correct light projection	on 181 eyes,
counting fingers close to face	on 43 eyes,
0.01 — 0.03	on 56 eyes,
0.04 — 0.06	on 16 eyes,
0.07 — 0.1	on 13 eyes,
over — 0.1	on 34 eyes

What were the results of the surgical treatment?

Successful results were obtained on 533 eyes (96%) out of 555 operated eyes. We consider successful the results of the cases of surgical treatment when the fornices have been restored and the normal position of the eyelids and complete closing of the eyelids have been achieved.

The fornices were restored on remaining 22 eyes (4%) but as we could not obtain complete closing of the eyelids we consider that the surgical treatment in these cases was not successful.

Thus, the total percentage of the success amounts to 96. Now let us analyse the results of the treatment depending upon the initial state of the operated eyes presented in Table 1 (See page 1311).

As the table shows the removal of partial symblepharons occupying up to 1/3 of the eyelid surface (99 eyes) resulted in 100% success. In cases with extensive and total symblepharons of one eyelid and extensive symblepharons of both the eyelids (308 eyes) successful results were obtained on 229 eyes, i.e. in 97.1%.

In case of symblepharons and ankyloblepharons of both eyelids (148 eyes) successful results were obtained on 135 eyes, i.e. in 90.6%.

These data show that our method of surgical treatment of symblepharons is quite effective and in majority of cases permits to remove even the gravest adhesions formed after eye burns.

The effective method of removing adhesions permitted us to perform widely the operations of keratoplasty to such patients. As our numerous observations showed lamellar keratoplasty proved to be the most effective method of keratoplasty in case of vascularized leucomas.



FIG 5 Patient S after the removal of symblepharon and peripheral lamellar keratoplasty on the right eye



FIG 6 Patient S Right eye after peripheral lamellar keratoplasty

cornea, total vascularized leucomas of both the eyes. Visual acuity equals to correct light projection on both the eyes (Fig 7). At first the symblepharon on the left eye was removed (Fig 8). Then total



FIG 7 Patient H. Extensive symblepharon of the upper lid overgrowth of scar tissue on the cornea of the left eye



FIG 8 Patient H. After the removal of symblepharon on the left eye

lamellar keratoplasty was performed. After the transplantation of the cornea the visual acuity on the left eye increased to 0.08. Observations lasted for two years (Fig 9).



FIG 9 Patient H. Left eye after total lamellar keratoplasty

the left eye (Fig 2) Then the operation of peripheral lamellar keratoplasty after our method was performed (N A Pouchkovskiy, 1955, 1960) The central part of the cornea became transparent after the operation Visual acuity equals 0.2 Observations lasted for 1.5 years (Fig 3)



FIG 2 Patient P Left eye after the symblepharon has been removed



FIG 3 Patient P Left eye after peripheral lamellar keratoplasty

Patient S 25 years old, case hist Nos 9081, 11520, 13397 Burn of both the eyes with melted metal 1 year ago Total symblepharon of both the eyelids and ankyloblepharon of the right eye, visual acuity equals to wrong light projection Lentic leucoma, secondary glaucoma of the left eye, visual acuity equals to light perception (Fig 4)



FIG 4 Patient S Total symblepharon and ankyloblepharon of the right eye

At first two basic operations were performed on the right eye to remove the symblepharons and then peripheral lamellar keratoplasty was performed after our method

The cornea corresponding to the pupil region became transparent due to the operation Visual acuity equals to 0.09 Observations lasted for 3 years (Figs 5, 6)

Patient K 22 years old, case hist Nos 29158, 32327 39055 36019 Three years ago — a burn of two eyes with lime Extensive symblepharon of the upper eyelid overgrowth of scar tissue on the



FIG 5 Patient S after the removal of symblepharon and peripheral lamellar keratoplasty on the right eye



FIG 6 Patient S Right eye after peripheral lamellar keratoplasty

cornea, total vascularized leucomas of both the eyes. Visual acuity equals to correct light projection on both the eyes (Fig 7). At first the symblepharon on the left eye was removed (Fig 8). Then total



FIG 7 Patient S Extensive symblepharon of the upper lid overgrowth of scar tissue on the cornea of the left eye



FIG 8 Patient S After the removal of symblepharon on the left eye

lamellar keratoplasty was performed. After the transplantation of the cornea the visual acuity on the left eye increased to 0.08. Observations lasted for two years (Fig 9).



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FIG 5 Patient S after the removal of symblepharon and peripheral lamellar keratoplasty on the right eye



FIG 6 Patient S Right eye after peripheral lamellar keratoplasty

cornea total vascularized leucomas of both the eyes Visual acuity equals to correct light projection on both the eyes (Fig 7) At first the symblepharon on the left eye was removed (Fig 8) Then total



FIG 7 Patient S Extensive symblepharon of the upper lid overgrowth of scar tissue on the cornea of the left eye



FIG 8 Patient K. After the removal of symblepharon on the left eye

lamellar keratoplasty was performed After the transplantation of the cornea the visual acuity on the left eye increased to 0.08 Observations lasted for two years (Fig 9)



FIG 9 Patient K. Left eye after total lamellar keratoplasty

The above data show that our method of removing symblepharons followed by keratoplasty makes possible to obtain the restoration of vision even in some patients with very grave consequences of eye burns, i.e. to obtain success in the patients whom as it seemed at first it was impossible to help.

Our numerous observations permit to recommend to use widely our method of removing symblepharons followed by optic lamellar keratoplasty in case of grave consequences of eye burns in the practice of ophthalmologists.

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## TRAITEMENT DES BRULURES DES YEUX

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Il existe beaucoup de moyens medicamentaires et operatoires pour traiter les brulures graves. On recommande à faire une section dans la conjonctive troublee sa separation. En appliquant ces operations nous n'avons pas obtenu ni bon ni tres mauvais resultats. Certain auteurs dans le but d'empêcher une commissure ainsi que a l'effet thérapeutique couvrent l'oeil brule par protheses en materiaux divers. Nous pouvons constater que lors des brulures graves aucuns prothèses n'empêchent les procedes de cicatrisation et le prothese est jete dehors, pousse hors de l'orbite. Nous avons essaye les protheses de differente forme: cuvettes d'Illogue, platines plastiques en verre, en caoutchouc, le pellicule ovalbumine, le papier etc.

Nous croyons que leur application est inutile et parfois meme aggrave le procede de brulure comme l'operation Denruegue car, selon nos observations dans le cas ou la muqueuse adhere la therapeutique complexe actuelle assure les meilleurs resultats.

Nous avons surveillé dans les conditions d'un stationnaire 724 malades ayant les brulures des yeux. En 92% c'étaient les brulures du 2nd et 3me degré, d'ailleurs 41% de malades avaient brûlures de deux yeux. Les brulures chimiques sont constatées en 78,9% de cas.

En analysant les resultats nous pouvons constater que l'administration du sang ou serum de sang par l'instillation et dans les cas plus graves par injection sous la conjonctive donne de bons resultats.

Nous nous appliqués un melange compose du sang, vasodilatateur, penicilline et le temps dernier — antibiotique imanine, substance anesthésique bloquant vitamine. En administrant un tel melange antibrulure il ne faut pas avoir une attitude banale, car la proportion des composants doit être variée selon la predominance de l'un ou de l'autre facteur au cours de procede de brulure.

En général la formation des foyers nécrotiques arrive tot au cours de premiers 3-5 jours. Evidemment cette formation est liée avec la formation de thrombus dans les vaisseaux sanguins. C'est pourquoi au cours de premiers 3-4 jours à coté d'autres moyens medicamentaires il est utile d'administrer les resorptives, les preparats empêchant l'accélération de vitesse de la coagulation du sang du type d'anti-coagulants.

The above data show that our method of removing symblepharons followed by keratoplasty makes possible to obtain the restoration of vision even in some patients with very grave consequences of eye burns, i.e. to obtain success in the patients whom at first it seemed it was impossible to help.

Our numerous observations permit to recommend to use widely our method of removing symblepharons followed by optic lamellar keratoplasty in case of grave consequences of eye burns in the practice of ophthalmologists.

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## A NEW OPERATION FOR FRACTURE OF THE OPTIC CANAL AND DISEASES OF THE ORBITAL APEX

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According to statistics published by the World Health Organization in 1962 the number of deaths by accidents has been increasing every year with the traffic accidents ranking first. It is said that more than 100,000 people die from traffic accidents every year.

In many traffic accidents head injuries especially, fractures of the base of skull present problems. In the field of ophthalmology the problems lie largely in the fracture of the optic canal. Statistics compiled by the Department of Ophthalmology of Osaka University (8) showed that the number of injuries to the optic nerve ranked top of all the other injuries sustained by traffic accidents.

The treatment of the fractures of the optic canal has not produced good results in the past. The major principle of treatment of this type of fracture has been decompression of the optic nerve. The conservative treatment may have successfully relieved hematoma or the cerebral concussion due to the fracture, but has often failed to improve vision, and sometimes led to blindness.

Craniotomy, one of the approaches used today, leaves a scar on the forehead and not infrequently causes headaches and may even result in fatality because the dura is incised and the chiasma is reached by elevation of the brain. This procedure however, merely permits the removal of the hematoma but it is difficult to remove the fragments. It permits at best, the removal of fragments only of the upper wall of the optic canal.

The intranasal operation is another approach to the problem. The optic canal can be reached through the nostril or the maxillary sinus. This operation however allows only a limited operative field and therefore the removal of fragments is difficult. The mucous membrane may remain uncleaned and often results in infection later. It is difficult to remove fragments completely by either method. Even though it is possible, only one quarter that is 90 degrees of the circumference of the optic canal can be explored and, there is always the risk of injuring the dura or causing infection.

I came to think of a new operative approach. That is to reach the optic canal by opening the frontal sinus, the ethmoid sinus and the

Un des problèmes dans le thérapeutique complexe des brûlures n'est une plus rapide et complète élimination du tissu nécrotisé, ce dernier diminue la gravité des iridocyclites et uvéites arrivant souvent. Pour éliminer les tissus nécrotiques, outre les méthodes mécaniques, dans les cas où la cornée n'est pas dérangée, nous avons commencé d'administrer le tripsine. Nous l'avons administré sous forme d'une solution 1%, dont le dissolvant était un tampon en phosphate avec  $\text{Ph} = 8,04$ .

Après avoir nettoyé les sections brûlées des tissus nécrotisés afin de stimuler les procédés de régénération, il est utile d'ajuster aux préparats les nucléotides produits de fission d'acides nucléiques, qui sont un des facteurs nécessaires pour le développement des cellules.

Touchant de la question d'application locale des corticostéroïdes, nous pouvons constater, que ces préparats ne sont pas utiles sur toutes les étapes du traitement des brûlures. Dans les cas où la défense inflammatoire est faible, les tissus inflammatoires, quand cette inflammation est si grave, qu'il faut administrer les vasodilatateurs, — ces préparats sont nocifs.

En période où il y a une réaction inflammatoire abondante, une vascularisation abondante, — leur administration est efficace.

Années dernières, sont publiés les travaux constatant que dans la cuir brûlée et le serum de sang naissent des autoanticorpuscules spécifiques. Il y a des preuves de la présence dans le serum du reconvalescent, ayant enduré la brûlure, des anticorpuscules relevant le complément en regard de l'anticorpuscule de brûlure. Alors, le serum de reconvalescent ayant enduré une brûlure, lors de son injection à un homme brûlé frais ou à un animal, doit exercer une action antitoxique.

Les travaux expérimentaux de l'institute des maladies ophthalmologiques à Odessa constatent, que le serum de sang des convalescents, ainsi que le serum de sang des lapins, immunisés d'une méthode certaine, — exercent une action thérapeutique lors de son injection au lapin, qui ont des brûlures des yeux.

Compte tenu de l'expérience positive en regard de la thérapeutique pathogénétique plus rationnelle de la brûlure, nous avons, le temps dernier, administré avec succès les transfusions du serum ou du sang des donneurs qui ont enduré une brûlure. L'auto-sang entrant dans le mélange lors de l'injection sous la conjonctive, nous avons remplacé par du sang ou du serum de sang du reconvalescent ayant enduré une brûlure, aux intervalles entre les injections nous avons instillé le serum de sang de mêmes donneurs.

On sait, que lors des brûlures des yeux les changements arrivent non seulement dans l'organe de vision, mais ils sont reflétés sur l'état général, la régulation nerveuse et endocrinienne se trouble, ce dernier doit être retenu lors de la sélection de méthodes du traitement des brûlures. Voilà pourquoi lors du traitement in loco il faut simultanément d'administrer le thérapeutique général.

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The treatment of the fractures of the optic canal has not produced good results in the past. The major principle of treatment of this type of fracture has been decompression of the optic nerve. The conservative treatment may have successfully relieved hematoma or the cerebral concussion due to the fracture but has often failed to improve vision and sometimes led to blindness.

Craniotomy, one of the approaches used today, leaves a scar on the forehead and not infrequently causes headaches and may even result in fatality because the dura is incised and the chiasma is reached by elevation of the brain. This procedure however merely permits the removal of the hematoma but it is difficult to remove the fragments. It permits at best the removal of fragments only of the upper wall of the optic canal.

The intranasal operation is another approach to the problem. The optic canal can be reached through the nostril or the maxillary sinus. This operation however allows only a limited operative field and therefore the removal of fragments is difficult. The mucous membrane may remain uncleared and often results in infection later. It is difficult to remove fragments completely by either method. Even though it is possible, only one quarter that is 90 degrees of the circumference of the optic canal can be explored and there is always the risk of injuring the dura or causing infection.

I came to think of a new operative approach. That is to reach the optic canal by opening the frontal sinus, the ethmoid sinus and the



sphenoid sinus along the upper medial corner of the orbit. This permits of a safe and satisfactory method for removal of fragments. It affords a wider operative field and eliminates the necessity of opening the dura.

As it required entry into the sinuses, I requested Dr. Shoji Niho, rhinologist, to examine the new method and to conduct the first operation.

The operation was more successful than originally expected. It was learned that this operation can be applied not only to the fractured optic canal but also to rhinogenous neuritis, traumatic or rhinogenous paralysis and orbital tumor, as it cuts open the orbital apex.

### METHOD OF OPERATION

The key points of the operation are described below. The operation of the maxillary sinus is not always necessary but may be advisable to prevent inflammation and to make further operation easy because the operation of the maxillary sinus often leads to a discovery of fragments which cannot otherwise be discovered clinically or roentgenologically. (Even in the case of rhinogenous neuritis or rhinogenous paralysis, operation of the maxillary sinus as a first step may be advisable, as such diseases are often caused odontogenously. In odontogenous cases, the mucous membrane is not usually affected, but osteomyelitis may develop and may require an operation of the maxillary sinus.) This operation may be done by the conventional method.

Following the opening of the maxillary sinus, it is advisable to open intranasally the ethmoid sinus and the sphenoid sinus as wide as possible. It will make the extranasal operation to be performed later easy. Care must be taken not to traumatize the lamina cribrosa. Otherwise, meningitis may follow.

The intranasal operation is followed by an extranasal operation. Our new method begins here. As first step the skin is cut from the nasal root into the eyebrow (Fig. 1-A). The operation proceeds to remove the mucosal lining of the frontal, ethmoid and sphenoid sinuses, and to remove the upper inner bony wall of the orbit as far back as the optic canal (Fig. 1-B, C).

During the operation, the patient may experience a sudden increase or decrease of vision. Thus, a local anesthesia is necessary, for the subjective response of restoration or diminution of vision during the operative procedure is of extreme importance. Operation under local anesthesia is possible in children. Care must be exercised not to traumatize the trochlea and the lacrimal sac when the lining of the frontal sinus is removed. The further posterior operation discloses the sphenoid sinus. Its location can be determined by X-ray examination.

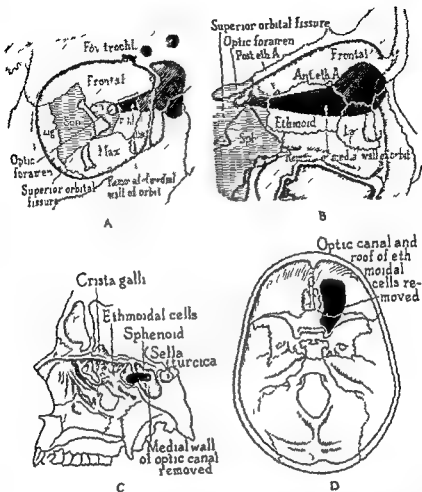


FIG 1 (A) Removal of shaded portion to enter the ethmoidal cells and the frontal sinus (B) Removal of the medial wall of the orbit to the distal end of the bony optic canal (C) Removal of the medial wall of the optic canal Shaded portion Grade I operation (D) Craniotomy Removal of the roof of the ethmoidal cells and of the optic canal Shaded portion Grade II operation

The anterior and posterior ethmoid arteries now become obstacles in reaching the posterior ethmoid sinus and it must be cut with great care for hemostasis before proceeding further. The optic canal will then be observed extending from the anterior lateral to the posterior medial on the upper wall of the sphenoid sinus or the ethmoid sinus. The anatomy of the optic canal varies. Fragments are removed in the case of fracture. If the fragments are not visible, the lower and the medial wall of the optic canal are removed.

When the injury is still fresh, the removal of fragments or the bony wall often results in the sudden increase of vision. Utmost care must be exercised not to traumatize the optic nerve.

This procedure allows of removal of half of the circumference of the optic canal and often suddenly increases vision, at which time the operation may be ended. This is our Grade I operation. If there is no subjective improvement in vision, we now begin to unroof the optic canal. This is our Grade II operation (Fig 1-D).

A craniotomy is performed opening the upper wall of the ethmoid and the sphenoid sinuses as far as the anterior clinoid process. The dura is elevated, care being taken not to traumatize the lamina cribrosa, the dura, or the optic nerve. Thus the upper, the lower and the medial wall of the optic canal can be removed. When the operation is over, sufficient drainage is instituted and antibiotics are given both locally and generally. Several weeks of bed rest is required.

The vision and the visual field which improved during the operation may deteriorate in the following week due to the operative reaction, but will be restored in several months.

Table I shows the period of observation after operation in 14 cases of fracture of the optic canal.

TABLE I — Cases of fractured optic canal

Case	Age (yr)	Sex	Days until Operation	Preoperative Vision	Postoperative Vision	Days After Operation
1	19	M	37	0	sl	1 yr
2	25	M	6	0 03 0 04	0 4	1 yr
3	30	M	52	0 01	0 1	1 yr 10 mo
4	31	M	263	0 1	0 6 0 7	2 mo
5	31	M	14	0 02	0 4	1 yr 5 mo
6	31	M	6	0 02	0 1	1 yr 1 mo
7	9	F	5	0	0 04	1 yr 4 mo
8	67	M	102	0	0	1 mo
9	16	M	12	10 cm/n d	0 1	5 mo
10	24	M	53	0 1	0 7	2 mo
11	17	M	16	0 06	0 3	4 mo
12	32	M	5	5 cm/n d	0 1	53 d
13	30	M	25	20 cm 2m/n d	70 cm 1 m/n d	84 d
14	19	M	164	0 006	0 03	140 d

From these cases we can conclude that the fresher the injuries, the better the results. This shows in Cases 1 and 7, where the vision of the persons without light perception was restored, although slightly.

However such visual recovery—the recovery from no light perception—is unusual. Therefore, in Case 7, six ophthalmologists confirmed the fact that the patient had no perception of light, but following the operation the patient demonstrated before the ophthalmologists at a Tokyo medical meeting that vision had been restored.

In contrast, as shown in Case 8, where the patient was operated 102 days after the injury, vision was not restored. It was also discovered that patients with good preoperative vision have a better chance of visual recovery even with traumatic optic atrophy.

This operation permits opening of the orbital apex and the bony optic canal and therefore can be applied to some other conditions. We happened to experience an unexpected improvement of paralysis of the extrinsic muscle when fragments were removed. This may be due to the decompression of muscles and nerves. For this reason, we applied this operation to the treatment of rhinogenous neuritis (3, 5, 9) and paralysis (1, 2, 3, 5, 7, 9) which were caused by the inflammation or compression of the orbital apex.

Table II shows nine cases of rhinogenous neuritis. Many serious cases are caused odontogenously and are apt to develop osteomyelitis and meningitis and therefore necessitate the extraction of teeth in some cases.

For example, in Case 7 the patient's life was saved but vision became worse. In cases 7, 8 and 9, the conventional intranasal operation was performed but having produced no satisfactory result, we resorted to our extranasal operation. This produced a good result. In Case 9 the patient with no perception of light for two weeks following the traditional intranasal operation had restoration of vision to 0.7 after our operation. Such recovery of vision from no perception of light seldom occurs in the conventional operation but in our operation success is not infrequent as indicated also in Cases 1 and 7 of the fracture cases. For this reason we felt that our operation has fairly good results.

In rhinogenous neuritis pus is not always evenly distributed in the sinuses. One sinus may be more seriously infected than others but infection must be *completely eliminated from all the sinuses* to prevent recurrence.

A histological examination of the bony wall of the optic canal removed at the time of rhinogenous neuritis revealed that noticeable inflammation penetrated from the mucous membrane through the bone of the optic canal almost to the optic nerve.

The operation for paralysis of ocular muscles can also be performed in a similar manner to decompress the muscles and nerves. That is to say, the sinuses must be cleaned in the case of rhinogenous

This procedure allows of removal of half of the circumference of the optic canal and often suddenly increases vision, at which time the operation may be ended. This is our Grade I operation. If there is no subjective improvement in vision, we now begin to unroof the optic canal. This is our Grade II operation (Fig 1-D).

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4	31	M	263	0 1	0 6 0 7	2 mo
5	31	M	14	0 02	0 4	1 yr 5 mo
6	6	M	6	0 02	0 1	1 yr 1 mo
7	9	F	5	0	0 04	1 yr 4 mo
8	67	M	102	0	0	1 mo
9	16	M	12	10 cm/n d	0 1	5 mo
10	24	M	53	0 1	0 7	2 mo
11	17	M	16	0 06	0 3	4 mo
12	32	M	5	5 cm/n d	0 1	53 d
13	30	M	25	20 cm 2m/n d	70 cm 1 m'n d	81 d
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TABLE II — Cases of rhinogenous neuritis

Case	Age (yr)	Sex	Preoperative Vision	Postoperative Vision	Other Symptom	Its result
1	54	F	r 0 02 l 0 03	r 0 5 l 0 3	r Ophthalmoplegia externa & Exophthalmus	cured
2	34	F	r 0 02 l 1 2	r 0 6 l 1 2	r Ophthalmoplegia externa	improved
3	18	F	r 1 2 l 0 6	r 1 2 l 1 2	l Ophthalmoplegia ext & Papilla edema	cured
4	30	M	r s 1 l 0 006	r s 1 l s 1	Odontogenous Headache	improved
5	7	F	r 1 0 l 0 03	r 1 2 l 1 2	Odontogenous l Papilla edema	cured
6	41	M	r 0 2 l 1 0	r 0 3-0 4 l 1 0	r Papilla edema	cured
7	40	F	r 0 7 l m m	r 0 9 l zero	Odontogenous l Ophthalmoplegia ext & Exophthalmus Meningitis	cured
8	19	M	r 1 2 l 10 cm/n d	r 1 2 l 1 1	l Papilla edema	cured
9	19	F	r 1 0 l 0 03	r 1 2 l 1 2	Odontogenous l Papilla edema	cured

paralysis In the case of fracture, the medial orbital wall shall be removed and the nerve of the extrinsic muscle shall be decompressed by gently striking the lower bone of the superior orbital fissure laterally with a hemostatic chisel The paralysis improves dramatically immediately following the decompression

This operation was found very effective in Case 1 of the fracture, Cases 1, 2, 3, and 7 of the rhinogenous neuritis and Case of the rhinogenous ophthalmoplegia ( ) This operation affords a visual examination of orbital apex and thus enables more effective operative procedure in the case of tumor or inflammation

#### THE OPTIC NERVE MUST BE TREATED WITH EXTREME CARE

I accidentally experienced this in the operation for retinal detachment, when I hooked and turned the optic nerve to craterize the

macular rent. Serious neuritis occurred followed by optic atrophy. We also learned that the vision diminished suddenly when the optic nerve was exposed and stimulated accidentally by pressing or poking during the operation for fracture and rhinogenous neuritis. We stopped traumatizing the optic nerve and vision was restored within 10 to 30 minutes.

Compared with other nerves the optic nerve is far more vulnerable. Optic atrophy which develops in sinus or brain surgery may have been frequently caused by rough handling of the optic nerve and not by damaging it as previously believed. For this reason, local anesthesia is the one of choice in operations involving the optic nerve.

Sinus diseases do not always affect all the sinuses. It can occur in a small section of the ethmoid sinus. Assuming that the optic nerve is very vulnerable, such trifling disturbance could cause blurred vision. If so, the diagnosis of rhinogenous neuritis becomes extremely difficult.

Very frequently, this operation may disclose the fragments which were not identifiable in the X-ray examinations, or may lead to a discovery of the sinusitis which cannot be diagnosed through clinical examinations.

## CONCLUSION

- 1 This operation jointly devised with Dr. Niho seems very effective and safe not only for the treatment of fractured optic canal but also for such diseases as affect the orbital apex such as rhinogenous neuritis, ocular paralysis or tumor.
- 2 The important points of the operation have been brought out.
- 3 Diagnosis of sinus diseases is difficult.
- 4 The optic nerve is sensitive and must be handled with care.

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# STRUCTURAL CHANGES OF THE OPTIC TRACT FOLLOWING UNILATERAL AND BILATERAL ENUCLEATION OF THE EYE BALL

GURGENIDZE R. V

(Tbilisi)

The structural changes of nerve fibres both in unilateral and bilateral enucleation of the eye ball develop all along the optic tract from the optic nerve to the 17th field for the brain cortex. Their study in a dynamic aspect permits to specify some points related to the course and location of the optic tract.

The basic mass of the optic nerve, the chiasm and the tract consists of afferent nerve fibres which in case of enucleation are liable to Wallerian degeneration and death. In comparatively early periods following enucleation, a small number of remaining axial cylinders are to be found which is also a pointer to the presence of afferent nerve fibres in the peripheral portions of the optic tract.

At first the crossed fibres of the optic nerve penetrate to an extent into the optic nerve on the opposite side and then proceed into the optic tract.

In the caudal part of the optic tract the crossed and uncrossed nerve fibres primarily occur in the form of separate bundles whereas in the cranial section of the tract they are more or less evenly intermingled. At the same time in the caudal section of the optic tract the uncrossed nerve fibres occupy the central area while the crossed fibres are located in the medial and lateral sections of this part of the tract.

Upon passing through the optic tract the afferent fibres of the optic nerve penetrate into the external geniculate body and into the superior colliculus.

The abovementioned fibres end at the round and multipolar ganglionic cells of the primary optic centres. The larger multipolar cells must represent the afferent neurons of the reflex arc of the optic tract.

The terminal of the central afferent neuron of the optic analyser must be in the external and internal granular layers of the 17th field of the brain cortex.

## PLASTIC ARTIFICIAL CORNEA—A FOURTEEN-YEAR STUDY

### Basic Principles Underlying Retention of Incompletely Covered Foreign Body in the Cornea

WILLIAM STONE, Jr, M D \*

Approximately one hundred and fifty years ago, before the advent of homotransplantation, several unsuccessful attempts were made to use alloplastic materials as replacements for the cornea. Little was done further until around 1950, when a few reports appeared on one or more cases of the use of plastic materials in either animal or human eyes.

The work presented here began fourteen years ago<sup>1, 2, 3, 4</sup> as a result of a phenomenon we observed during the second World War: several pilots were seen with small fragments of methyl methacrylate embedded in their corneas; these were very well tolerated and did not extrude. We felt, therefore, that it might be possible for the cornea to tolerate larger pieces of this transparent plastic equally as well. We had had experience with incompletely covered, post enucleation implants and were confident at that time that such an implant could be maintained in the body without extrusion.

#### EARLY EXPERIMENTATION

Various types of through and through discs were tried first (Fig. 1). Approximately 25 shapes and sizes were fabricated, with



FIG. 1 Various types of through and through plastic discs placed as full thickness implants in rabbit corneas 14 years ago. All extruded within one to two weeks.

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This work is being supported by the Massachusetts Lions Eye Research Fund, Inc., Office of Naval Research grant #1173(01) and National Institutes of Health grant #B-1027.

assorted appendages at the edges to anchor the implant in corneal tissue. All of these extruded in a short time.

Following this, in 1949 a disc (Fig 2) shaped to the contours of the rabbit cornea with holes in a peripheral skirt for tissue ingrowth was placed intralamellarly in rabbit corneas. Figure 3 shows a portion of cornea from which a disc of this type was teased. The projections

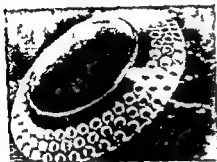


FIG 2 Disc shaped to contour of rabbit cornea with holes in peripheral skirt for tissue ingrowth. Placed between the lamellae (1949)

FIG 3 Rabbit cornea after an intralamellar implant (as seen in fig 2) had been teased from it. Projections A and B are collagenous plugs of corneal tissue which grew through the peripheral fenestrations and held the implant firmly in place.



FIG 4 Intralamellar implant in cornea of Rabbit #83 with circular opening in anterior layer of cornea down to plastic anterior chamber can be seen clearly. Photograph was taken 12 months post operative. (Central opening occurred inadvertently as a result of premature rupture of sutures several days after the operation.)

(A & B) are collagenous plugs of tissue which grew through the peripheral fenestrations and held the implant firmly in place ensuring its stability.

#### EXPOSURE OF ANTERIOR SURFACE

The second phase of the work began inadvertently. In one rabbit after an intralamellar disc had been placed, the sutures on one side broke loose several days post-operatively and the anterior layer of cornea receded from the central area of the disc (Fig 4). This disc

remained exposed centrally to the natural death of the animal, one year after surgery. The implant did not move and the anterior chamber was at all times clearly visible through the anterior hole.

We were persuaded that this exposure could be easily reproduced by deliberately opening the anterior layer, but it took two years to repeat the experiment, namely, to permanently maintain a corneal opening anterior to a plastic disc.

The feature responsible for maintaining the patency of an anterior trephine hole was not immediately apparent. Figure 5 illustrates the typical progression of tissue growth across the exposed surface. After a hole was trephined, whether large or small, within several days a salmon colored area of tissue would appear at the edge of the trephine hole and then gradually, over a period of approximately 25-52 days, the tissue area would expand until it completely filled the opening. The diameter of the trephine hole did not materially affect the speed



FIG. 5 Closing of trephine hole in anterior corneal layer in front of a plastic disc (Rabbit #21 Experiment 2) A Two days post operative. There is slight engorgement of vessels. B Eight days post operative. A distinct salmon coloring can be seen at edge of hole. C Twenty one days post operative. The salmon colored edge has nearly obliterated the hole. D Twenty nine days post operative. The hole is completely closed.



with which it closed, for an 8 mm hole closed in 27 days while on an average 4 mm holes closed in 40 days. The overall average closing time of these anterior trephine holes was 37 days in 44 rabbit eyes (Table I)

TABLE I — *Time of closure of trephine hole in corneal layer anterior to plastic disc as related to size of trephine opening*

Number of Rabbits	Size of Trephine	Maximum Days Open	Minimum Days Open	Average
4	4 mm	50	30	40
19	5 mm	52	20	38
14	6 mm	50	29	38
6	7 mm	50	35	43
1	8 mm	27	27	27
Overall Average				37

It was thought that possibly the time lapse between implantation of disc and incision of anterior hole might be the determining factor. Table II shows the results when holes were placed at various intervals post implantation. Trephine holes were made at periods ranging from one week to two years after the placing of the disc. In 62 rabbit eyes irrespective of the extent of the interval between the two operations the holes closed in approximately 37 days.

TABLE II — *Interval between implantation procedure and placing of anterior trephine hole in relation to closure of trephine hole*

Number of Rabbits	Time After Original Operation Trephine Placed	Time of Closure After Trephine Placed		
		Maximum	Minimum	Average
29	Trephined during placement of implant	52 days	31 days	43 days
4	7 to 30 days	50 days	25 days	36 days
19	1 to 6 months	43 days	20 days	37 days
13	6 months to 1 year	48 days	28 days	37 days
4	1 to 2 years	50 days	30 days	40 days

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TABLE III — Diagram of various operative procedures used in cutting a hole in corneal layer anterior to Plastic Disc and results—(contd.)





Exp Number	Operative Procedure	Rabbit Number	Exp Number	Time of Closure after op	Extrusion after Placement of implant
				Days	Days Post op
19	Trepined past and with evacuation first row holes 	20	2	30	199
20		25	3	40	—
21		223	2	20	—
22		234	3	22	—
23	Cruciate incision with flaps sutured under 	15	6	40	—
24		51	5	26	—
25		61	2	51	—
26		66	1	—	51
27	Very superficial Incision 	234	1	40	—
28		58	1	—	130
29		80B	1	—	14
30		90	1	—	90
31	Thin thick Incision 	61	1	47	—
32		62	1	Open 8 Mon PO	—
33		63	1	—	72



Table III describes the types of operative procedures which were tried in an effort to produce a permanent opening in front of the implant. It was not until Rabbit #62 that a hole was obtained which

TABLE III — Diagram of various operative procedures used in cutting a hole in corneal layer anterior to Plastic Disc and results









Item Number	Operative Procedure	Rabbit Number	Exp Number	Time of Closure after op	Extrusion after Placement of implant
1	Straight Cut 	Experiments with this operative procedure not included. Majority of experiments in Charts 1 and 2 employed this method and are noted there.			
2	Angle Cut 	21	1	Days 28	Days Post op —
3		25	2	42	—
4		30	1	35	—
5	Undermined with Angle Knife 	29	1	40	—
6		29	2	40	
7		30	2	30	
8		42	1	33	
9	Trophined past first row of holes 	15	2	48	—
10		227	1	41	130 20 30 90 — 114
11		45	1	38	
12		46	1	—	
13		48	1	—	
14		49	1	33	
15		50	1	—	
16		51	1	45	
17		52	1	45	
18		54A	1	36	

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24		51	5	26	—
25		61	2	51	—
26		66	1	—	51
27	Very Superficial Incision 	244	1	40	—
28		58	1	—	130
29		80B	1	—	14
30		50	1	—	90
31	Thin thick Incision 	61	1	47	—
32		62	1	Open 8 Mon PO	—
33		65	1	—	72

remained patent for longer than 60 days (Fig 6) In this rabbit the center of the disc had been thickened (approximating an anterior projection) and it was found that the anterior trephine hole remained open indefinitely, the eye of the rabbit staying white and quiet



FIG 6 Rabbit #62 The first cornea in which a disc with an anterior projection was placed (Oct 1953) The thickness of the anterior projection was 1.5 mm The hole remained patent to the natural death of the animal 1 year 10 months post operative

FIG 7 Implant with central anterior projection and peripheral skirt for intralamellar insertion. Peripheral holes are for the ingrowth of tissue to prevent migration of the implant

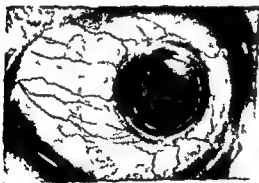


FIG 8 Implant (as seen in figure 7) which remained in rabbit cornea for 4 years 3 months to natural death of rabbit (The life span of the rabbit species limits the period of observation)

The type of disc seen in figure 7 was used at that time. It has a central anterior projection, a peripheral skirt which goes between the lamellae, and peripheral holes for the ingrowth of tissue. Figure 8 shows a disc of this type in a rabbit cornea for four years three months post implantation, the maximum length of time we have kept a disc in place. The life span of the animal was the only deterrent to a longer implantation period.

## ANTERIOR PROJECTION

The experiments conducted to determine the optimum diameter of anterior nubbin and its optimal height are listed in Table IV. It was found that the diameter of the projection was not influential in maintaining the implant in place and had very little to do with prevention of tissue overgrowth.

TABLE IV — Diameter and height of anterior projection in relation to patency of anterior trephine hole\*

Width in mm	NUBBIN	Height in mm	Number of Rabbits	Results
5	×	1.25	12	Open
5	×	1.00	13	Open
4.5	/	1.00	3	Open
4.5	×	.7	1	Closed
4	×	1.00	2	Open
4	/	.75	3	Closed
4	/	.6	2	Closed
3.5	/	.7	1	Closed
3.5	/	.5	2	Closed
			<hr/> 39	

\* These figures also demonstrate that the width of the anterior projection is not consequential to retention of implant. An implant with a 5 mm wide projection is maintained in place as readily as one with a 3.5 mm wide projection. The height of the projection nevertheless was critical in preventing closure of the anterior trephine hole. A projection 1 mm or more in height always prevented tissue overgrowth and a projection less than .75 mm high always permitted overgrowth and closure.

The height of the nubbin was the controlling factor. A nubbin less than .75 mm above the anterior surface of the disc permitted overgrowth in nearly every case while anything higher arrested the tissue's progress. Minute variations in height were critical.

Pegs of tissue which grew into the peripheral skirt can be seen in Figure 9, an histological cross section of a cornea after the disc had been dissolved out. Figure 10 (A & B) presents a high magnification of the connective tissue which invaded peripheral fenestrations and it is apparent that no epithelial cells continued with the tissue. Figure 11 (A & B) shows the structure of the tissue at the edge of the anterior



FIG 9 Photomicrograph of cross section of cornea after disc has been dissolved out. Cut edge of anterior trephine hole and pegs of tissue which grew through peripheral fenestrations can be seen.

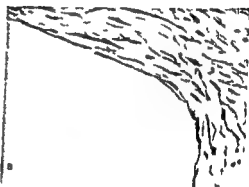


FIG 10 Photomicrograph showing connective tissue which invaded peripheral holes in skirt (A). Note that no epithelial cells grew through the holes (B).



FIG 11 Photomicrograph of corneal epithelial cells showing increase to 16-18 cell layer as they grow around the cut edge of anterior trephine hole (B) and reduction to 2-3 cell layer as they approach the area of proliferating connective tissue in region of fenestrations (A).

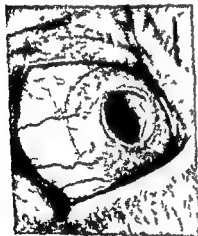
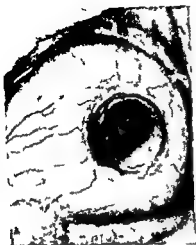


FIG 12 Rabbit cornea with plastic discs inserted intralamellarily with anterior trephine holes in place up to 4 years 3 months (to the natural death of the animal) A In place 4 years 3 months Rabbit #92 B In place 4 years Rabbit #197 C In place 3 years 10 months Rabbit #242 D In place 3 years Rabbit #221 F In place 2 years 9 months Rabbit #128



trephine hole. The epithelial cells pyramid to approximately 16-18 cell layers in thickness as they come around the hole (Fig 11B) and immediately, in the posterior side of the anterior layer, they reduce to 2-3 cell layers in thickness and, as they approach the area of the proliferating connective tissue in the region of the peripheral holes, reduce to a one cell layer and then stop (Fig 11A).

A series of implants in rabbit corneas for up to four years and three months are shown in figure 12. Table V is a chart of the implants which have remained in place with patent anterior trephine holes to the natural death of the animal. It is now felt that, barring infection (which seldom occurs in our animals), an implant placed as described will remain in place indefinitely with a patent anterior trephine hole.

#### FABRICATION OF IMPLANT

We also found that each individual rabbit eye must be molded and the disc made to the exact conformation of the cornea or pressure necrosis and extrusion will result.

Also, polishing materials cannot be used on the optical surfaces of the plastic corneas because microscopic bits of polishing materials will become embedded in the plastic, leading to foreign body reaction. The optical surfaces must, therefore, be molded to polished steel dies.

#### CLARITY OF POSTERIOR SURFACE

In the majority of cases, if the procedure of lamellar dissection is accomplished with an operating microscope, posterior clarity will be realized if dissection is made down to Descemet's membrane and if Descemet's membrane itself is not too opaque.

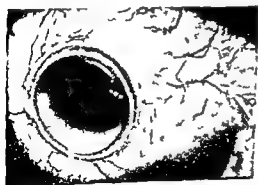


FIG 13 A crescent of opacification of the posterior corneal layer behind the anterior projection is visible. This opacity was caused by malapproximation of the disc in the periphery. The central portion remained clear.

In figure 13 it is seen that the central portion where the plastic comes in contact with the back surface of the cornea remains perfectly transparent. Where there was a slight peripheral malapproximation, fibroblastic tissue grew in and caused opacification, but the central portion remained clear.

TABLE V — *Implants with anterior trephine holes patent to natural death of Rabbit*

<i>Time Interval</i>	<i>Rabbit #</i>	<i>Length of Time Open</i>
4 years and over (3 rabbits)	92	4 years 3 mos
	259	4 years
	192	4 years
3 years to 3 years 11 mos (4 rabbits)	247	3 years 10 mos
	210	3 years 1 mo
	145	3 years
	221	3 years
2½ years to 3 years (4 rabbits)	266	2 years 10 mos
	128	2 years 9 mos
	231	2 years 8 mos
	68	2 years 10 mos
2 years to 2½ years (4 rabbits)	280	2 years 3 mos
	82	2 years 3 mos
	83	2 years 3 mos
	167	2 years 2 mos
1½ years to 2 years (8 rabbits)	45	1 year 10 mos
	62	1 year 10 mos
	123	1 year 9 mos
	102	1 year 8 mos
	226	1 year 8 mos
	93	1 year 8 mos
	211	1 year 6 mos
	224	1 year 6 mos
	225	1 year 5 mos
	69	1 year 3 mos
1 year to 1½ years (8 rabbits)	202	1 year 3 mos
	227	1 year 2 mos
	85A	1 year 1 mo
	46	1 year
	101	1 year
	104	1 year
	154	11 mos
	113	11 mos
	196	11 mos
	87	10 mos
6 months to 1 year (15 rabbits)	206	10 mos
	201	10 mos
	81	10 mos
	269	10 mos
	163	10 mos
	198	9 mos
	271	9 mos
	164	9 mos
	73	8 mos
	66	7 mos
	100	7 mos
		7 mos



An implant (Fig 14) with a definite recess to provide space for fibrin to enter and to allow more fibroblastic proliferation was tested. The posterior layer opacified.



FIG 14 Disc with recess in posterior portion of central projection. This created space for fibroblastic proliferation and caused posterior opacification.

If there is good approximation between the posterior layer of the implant and the posterior layer of the cornea, there will be no fibroblastic proliferation. The transparency of the posterior portion of the graft depends upon the pressure which is exerted on the posterior layer by the back surface of the plastic.

Therefore, it would seem that a posterior trephine hole will not be required in the majority of human cases and it will not be necessary to disturb the anterior chamber. This will reduce the risk of infection and increased tolerance of the implant.

When there is fibroblastic proliferation or when Descemet's membrane is opaque, a posterior trephine hole will be necessary. This must be placed only when several months post implantation, tissue has grown into peripheral holes (anchoring the implant) and epithelium has grown around the anterior trephine hole (sealing off the anterior chamber from fluid loss and bacterial invasion).

Rabbits with the artificial cornea implanted and anterior trephine holes and posterior trephine holes open for varying periods are shown in figure 15. Figure 16 is a histological cross section showing endothelium which grew around the edge of the posterior trephine hole to the area of the peripheral holes (where ingrowth of connective tissue had taken place) and stopped.

If the posterior trephine hole stays patent for ten days, it will remain open indefinitely. It is necessary to heparinize the animal to prevent the precipitation of fibrin in the posterior trephine hole. If this is averted, a matrix will not be laid down for the overgrowth of connective tissue.



FIG. 15 Rabbit corneas with plastic discs and central anterior and posterior trephine holes. A The anterior trephine hole remained open 2 years 10 months the posterior trephine hole remained open 2 years 5 months to the natural death of the animal (Rabbit #68). B The anterior trephine hole remained open 2 years 3 months 14 days the posterior trephine hole remained open for 1 year 10 months 22 days to the natural death of the animal (Rabbit #83). C The anterior trephine hole remained open for 1 year 3 months the posterior trephine hole remained open 1 year 10 days to the natural death of the animal (Rabbit #69). D The anterior trephine hole remained open for 1 year 25 days the posterior trephine hole remained open for 9 months 27 days to the natural death of the animal (Rabbit #104). Traumatic cataract is visible through the posterior opening. E Anterior trephine hole remained open for 1 year 4 days posterior trephine hole remained open for 9 months 4 days to the natural death of the animal (Rabbit #46).

### TREPHINE INSTRUMENT

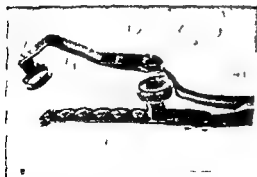
An instrument was designed to cut the posterior trephine hole (Fig 17 A & B). It consists of a circular cutting blade motivated by a series of watch gears which are turned by a knob from the outside. The lower arm of the instrument goes behind the plastic after an



FIG 16 Photomicrograph of posterior trephine hole in posterior layer of rabbit cornea showing endothelial cells migrating around cut edge and stopping at fibroblastic tissue proliferating into peripheral holes



FIG 17 A Instrument used for cutting trephine hole in rabbit cornea posterior to plastic disc a month or more after implantation B Enlargement shows trephine cutting blade which is placed in the anterior chamber through incision at edge of disc. It is motivated remotely by a knurled knob through a series of watch gears. The one month period between original operation and posterior trephine procedure permits sealing of wound by fibroblastic tissue and epithelium and prevents bacterial invasion and leakage of aqueous



incision at the edge of the disc and the upper arm goes in front of the plastic. The blade is then rotated by turning the knurled knob on the outside. Figure 15E is a posterior trephine hole seen from an oblique angle so that the cut edge of the hole is visible.

## IMPLANT MATERIAL

Figure 18 is the formula for the conversion of methyl methacrylate monomer to methyl methacrylate polymer. Incompletely purified and non standardized methyl methacrylate produced varying results in different animals, some of the plastic produced severe reactions and some minimal reaction. In different batches from the same manufacturer there was variation. Inconsistent results were even obtained from different sections of the same plastic rod.

The results were dependent upon the amount of trace impurities in the material, the amount of accelerator, inhibitor etc. which was present and whether or not pre polymerization had taken place. Hydroquinone, a common inhibitor, produces a severe reaction in the cornea of rabbits.

FIG 18 Polymerization reaction of methyl methacrylate with benzoyl peroxide as accelerator. If in completely polymerized monomer products severe reaction when implanted in cornea.

## POLYMERIZATION OF METHYL METHACRYLATE



Because impurities and additives are present in commercial methacrylate we have had to purify our own monomer and standardize polymerization in order to get consistent results.

As an aside here, it is felt that many of the reactions which have occurred with plastics placed in the anterior chamber to replace cataractous lenses have been a result of poor purification and standardization of the plastics which were used.

At the present time we are investigating the synthesis of a new type of plastic which is hydrophilic which permits absorption and transference of water through its matrix to approximately 40-70% of its weight and has a high diffusion coefficient for oxygen and  $\text{CO}_2$  (Fig. 19). This by the way should be more physiological than methyl methacrylate and will produce even better results.

## SYNTHESIS OF HYDROPHILIC POLYMER

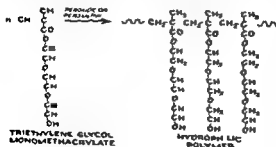


FIG 19 Synthesis of hydrophilic polymer which permits absorption of water and transference through its matrix to approximately 40-70% by weight. It has a high diffusion coefficient for oxygen and  $\text{CO}_2$ . Experimental work is being done with this at the present time in the Ophthalmic Plastics Laboratory.

## TREPHINE INSTRUMENT

An instrument was designed to cut the posterior trephine hole (Fig 17 A & B). It consists of a circular cutting blade motivated by a series of watch gears which are turned by a knob from the outside. The lower arm of the instrument goes behind the plastic after an



FIG 16 Photomicrograph of posterior trephine hole in posterior layer of rabbit cornea showing endothelial cells migrating around cut edge and stopping at fibroblastic tissue proliferating into peripheral holes

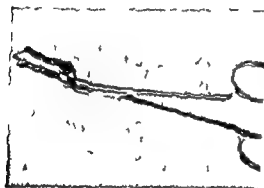
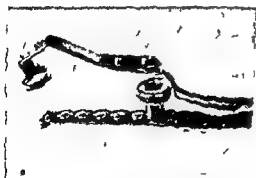


FIG 17 A Instrument used for cutting trephine hole in rabbit cornea posterior to plastic disc 7 months or more after implantation B Enlargement shows trephine cutting blade which is placed in the anterior chamber through incision at edge of disc. It is motivated remotely by a knurled knob through a series of watch gears. The one month period between original operation and posterior trephine procedure permits sealing of wound by fibroblastic tissue and epithelium and prevents bacterial invasion and leakage of aqueous



incision at the edge of the disc and the upper arm goes in front of the plastic. The blade is then rotated by turning the knurled knob on the outside. Figure 15F is a posterior trephine hole seen from an oblique angle so that the cut edge of the hole is visible.

sarcomata and cancers. In general a high rate of remission was obtained and the unpleasant symptoms of malignant disease have been relieved. Some authors have reported good results lasting over three years.

If I ever wanted to help my patients I had no other choice than the chemotherapy for the disease of my patients were bilateral cancer metastases of the eyes which at least in one patient identical with other proved metastases in her body.

What could have been more useful in these two cases — to operate or give an X Ray treatment?

The first case concerned 35 year old woman who had been referred to me by a colleague on the 23rd of April 1960 (more than  $2\frac{1}{2}$  years ago) because of a rapidly developing detachment of retina in her right eye. Examination showed a white infiltration of the whole central area of 'Choroid' with a slight detachment of retina in the upper nasal quadrant. Its surroundings showed some grey white areas with a prominence upto 3 D. no haemorrhages nor any signs of inflammation were seen in the retina. The corrected vision was 0.6 the picture was that of a metastatic carcinoma. The diagnosis being based on the fact that she had had a histologically verified carcinoma removed  $2\frac{1}{2}$  years previously followed after 2 years by lymphatic recurrences of the same histological nature which had been removed and radiational treatment given.

The patient, who was very cachectic refused treatment with Endoxan but shortly thereafter developed a similar metastases in the left eye. Visual acuity sank to R.E. 0.1 and L.E. 0.3. Treatment with Endoxan 100 to 200 mgm every second day intravenously was commenced however she lost weight, ran a temperature while the, leucocytic count fell from 5,000 to 1,270. The treatment was therefore stopped. Her general condition rapidly recovered and ten weeks later she left the hospital. The tumours had disappeared from both eyes leaving greyish white pigmented areas and the visual acuity in each eye was normal. Since she left the hospital she has received ten injections of Endoxan intravenous at two day intervals and one or two tablets of Endoxan or Miltarson (0.5 gr) daily by mouth her blood count being periodically checked. Now  $2\frac{1}{2}$  years later she is well full of energy and at work. There is no recurrence of the original tumour or metastases and the vision is normal. How long this will last is of course unknown.

The second case concerns of sixty year old and stout woman who had a radical mastectomy for histologically verified carcinoma. Since then she had several radiational treatments as a precaution and seemed to have been cured. Suddenly two years ago, she developed bilateral proptosis with diplopia. X Rays showed neoplastic metastases in the skull. Daily intravenous injections (200 mgm) of Endoxan were given. In the following ten days the leucocytic count fell from 8,800 to 5,000. The exophthalmos was less and the diplopia had disappeared. For a

## CHEMOTHERAPY OF OCULO ORBITAL CARCINOMATOUS METASTASES

PROF DR HANS SCHMELZER

(Bamberg)

The question of chemotherapy of malignant tumours is still very much in dispute, but is increasing in significance year by year. Even a scientist as Prof H. K. Bauer, Heidelberg, says that we are only able to cure about 18% of all cases of cancer by operation and X Ray treatment with a follow up period of at least five years. It follows that the importance of chemotherapy must be recognised.

I do not wish to enter into the local therapy of malignant tumours as recommended by Domagk, after which a special kind of "Loststoff" (E 39 "Bayer") is injected into the surroundings of malignant tumours. On this subject, Pillat and others in many countries have already reported, nor do I wish to discuss the method by Schliephake of irradiation of the hypophyseal hypothalamic system with which he was able to stop or control the growth of malignant tumours in more than eighty patients, so that several of them were able to work again.

I will, however, report on two patients on whom I obtained extremely good results up to the present by the intravenous injection of the cytostatic "Endoxan". The first was a case of bilateral metastatic carcinoma of the choroid (with secondary serous detachment) which occurred after surgical and X Ray treatment of a cancer of a breast, the second case showed a rapidly increasing bilateral exophthalmus due to retrobulbar metastatic carcinomata which also occurred after an amputation and X Ray treatment of a cancer of the breast some years previously.

The ideal chemotherapy depends on the elaboration of a cancerotoxic substance, active at the site of the growing tumour of sufficient selectivity that it affects as few as possible of the body cells and only restrains the growth of neoplastic cells. This is the fundamental problem on which cytostatics have hitherto failed, as for instance the Athyleniminchinon of Domagk's E 39 soluble and substance No. 3231 that Liegl used on a case similar to mine a year ago.

A number of publications have appeared about the effect of Endoxan therapy on all kinds of malignant tumours and blood diseases. Some of these publications sound rather pessimistic. One author even stated that in the field of chemotherapy our knowledge is still at the "ice age stage". Others again report good results, especially lymphatic (not myeloid) Leukaemia, Hodgkins disease and a number of

sarcomata and cancers. In general a high rate of remission was obtained and the unpleasant symptoms of malignant disease have been relieved. Some authors have reported good results lasting over three years.

If I ever wanted to help my patients I had no other choice than the chemotherapy, for the disease of my patients were bilateral cancer metastases of the eyes which at least in one patient identical with other proved metastases in her body.

What could have been more useful in these two cases — to operate or give an X Ray treatment?

The first case concerned 35 year old woman who had been referred to me by a colleague on the 23rd of April, 1960 (more than 2½ years ago) because of a rapidly developing detachment of retina in her right eye. Examination showed a white infiltration of the whole central area of Choroid with a slight detachment of retina in the upper nasal quadrant. Its surroundings showed some grey white areas with a prominence upto 3 D. no haemorrhages nor any signs of inflammation were seen in the retina. The corrected vision was 0.6, the picture was that of a metastatic carcinoma. The diagnosis being based on the fact that she had had a histologically verified carcinoma removed 24 years previously followed after 2 years by lymphatic recurrences of the same histological nature which had been removed and radiational treatment given.

The patient who was very cachectic, refused treatment with Endoxan but shortly thereafter developed a similar metastases in the left eye. Visual acuity sank to R.E. 0.1 and L.E. 0.3. Treatment with Endoxan 100 to 200 mgm every second day intravenously was commenced however she lost weight, ran a temperature while the leucocytic count fell from 5 000 to 1,270. The treatment was therefore stopped. Her general condition rapidly recovered and ten weeks later she left the hospital. The tumours had disappeared from both eyes leaving greyish white pigmented areas and the visual acuity in each eye was normal. Since she left the hospital she has received ten injections of Endoxan intravenous at two day intervals and one or two tablets of Endoxan or Mitarsol (0.5 gr) daily by mouth her blood count being periodically checked. Now 2½ years later she is well full of energy and at work. There is no recurrence of the original tumour or metastases and the vision is normal. How long this will last is of course unknown.

The second case concerns of sixty year old and stout woman who had a radical mastectomy for histologically verified carcinoma. Since then she had several radiational treatments as a precaution and seemed to have been cured. Suddenly two years ago she developed bilateral proptosis with diplopia. X Rays showed neoplastic metastases in the skull. Daily intravenous injections (200 mgm) of Endoxan were given. In the following ten days the leucocytic count fell from 8,800 to 5 000. The exophthalmos was less and the diplopia had disappeared. For a



further two weeks, the intravenous injections were given every second day. Altogether the patient was given 9.8 G of Endoxan intravenously and in the intermediate periods 1 to 2 tablets of Endoxan by mouth daily.

She maintained her treatment for over one year and then allowed it to lapse. Thereupon, the exophthalmos recurred, to disappear, however, with further injections of Endoxan, the leucocytes meantime falling from 7,200 to 3,100. The patient remained well until four weeks ago, when she complained of pains in her back. X-Ray examination revealed two metastases in the vertebral column in the lumbar region. After approximately three weeks and half of clinical treatment with Endoxan as well as a 'blood transfusion' and Anabolate the patient had recovered so far that she could walk again by herself and we could send her home. On the X-Ray taken on the day she left the hospital one can clearly recognise the beginning of "Ossification" of the destroyed part of the bones as a sign of regeneration. How long, however, this will last is questionable.

This case of multiple metastases — among them two retrobulbar occurring eleven years after an initial operation and subsequent radiational treatment shows how well and rapidly these malignant tumours respond to Endoxan.

The question arises whether these recurrences could have been prevented if one had immediately supplemented the operative and radiological treatment with Endoxan treatment or other form of chemotherapy?

I consider the communication of these cases important because each of us may be asked to help in such desperate cases. Further, operation is without any prospect and the X-Ray treatment very problematical in its results.

The result with the Endoxan treatment I obtained so far with my patients provides a possibility to help even if it is only temporary.

I hope to inform you of the further development of these two cases at a later date.

## EXPERIMENTAL AND CLINICAL RESEARCH ON RIGIDITY OF THE EYE

NESTEROV, A. P. (*Amblyop*)

Experimental investigations were carried out on 26 enucleated eyes. For the measurement of the ophthalmotonus a set of Maklakov's applanation tonometers was used, with weight of 5, 10, 15 and 20 grams and an impression tonometer of the Schiotz's type.

The changes in ophthalmotonus initiated by the application of a tonometer to the eye were registered simultaneously by means of a highly sensitive electronic manometer connected with a registering potentiometer.

The data thus received were compared with the results of a clinical research on rigidity, carried out by means of a set of Maklakov's applanation tonometers on 203 eyes and with the help of Schiotz's electronic tonometer on 145 eyes.

When applanation tonometers were used the coefficient of rigidity constituted on average 0.0186 (0.0080 to 0.0410), and the average value of elasto rise (after S. F. Kalfa) was  $9.7 \pm 4.3$  mm of Hg. The Schiotz's tonometer gave slightly bigger values of the coefficient of rigidity which on 145 eyes equalled to  $0.0239 \pm 0.0138$ .

The coefficient of rigidity as well as the 'elasto rise' changes along with alteration of the ophthalmotonus level.

The author suggests to use the conception of 'standardized elasto rise'. By this term one understands the difference (in mm of Hg) between the readings of two tonometers of different weight applied to an eye with the average value of ophthalmotonus (16 mm of Hg).

An interpolation formula is suggested for standardizing. The relation between 'standardized elasto rise' and rigidity of an eye is still being discussed.

# CONJUGATED ESTROGEN IN PROPHYLAXIS OF SECONDARY HYPHEMA

J G GILLAN

Presented at the International Congress of Ophthalmology  
New Delhi — December 1962

(Read by Dr P K Basu, at the Author's request)

The present article is the third of a series of studies conducted by the author in an effort to discover and reduce the number of secondary haemorrhages following direct and non penetrating injury to the eye. Because haemorrhage into the anterior chamber can be checked so easily and quickly, this was chosen as a good guide from the clinical point of view.

In the first article <sup>1</sup> an effort was made to study the complications associated with hyphema and the medical treatment. An introduction to the use of conjugated estrogen was made.

In the second article, 70 cases of hyphema treated by the author were analyzed <sup>2</sup>. In this 35 cases were treated conservatively and 35 by the use of conjugated estrogen. A considerable reduction in the incidence of secondary haemorrhage was noted in those cases treated with the conjugated estrogen.

This series has now been increased to 85, in which the 35 previously described as controls were again used as controls while those cases having conjugated estrogen were divided into 15 which had oral preparation and 35 which had intravenous administration of the hormone. The clinical results are summarised in the attached table.

Clinical Results	No of Cases	Sec Haem	Sec Glaucoma	Visual Loss
I Conservative Medical Therapy Alone	35	9	4	3
II Conservative Care Plus Oral Estrogen	15	1	1	1
III Conservative Care Plus IV Estrogen	35	1	0	1

The cases having oral estrogen had Premarin tablets 1.25 mg given three times a day during their stay in hospital with hyphema. Those treated with intravenous estrogen had the clinical dose of 20 mg given intravenously on admission and in certain cases where haemorrhage might be imminent another intravenous dose as required. The present treatment which is being used is to give 20 mg intravenously on admission. A similar dose on the third day and a similar dose on the fifth day if the hyphema has not completely subsided. In children where this intravenous administration is too difficult, intramuscular Premarin can be given of 10 or more milligrams each dose.

#### INVESTIGATION OF ACTION

In view of the clinical benefit in preventing secondary haemorrhage an effort was made to study the action of the conjugated estrogen in human subjects. Schiff and Burn<sup>3</sup> had discovered that conjugated estrogen given to hamsters intravenously, could produce a marked change in the ground substance of blood vessels. It therefore seemed feasible that similar changes should be possible to demonstrate in humans. A simple experiment therefore, was devised. During cataract surgery the author normally does a peritomy prior to making a corneal scleral section. It was therefore perfectly easy to remove a small piece of conjunctiva at the first operation.

Three groups of cases were examined. Six patients were operated upon seven to eight days after the first cataract extraction and during this period they were given oral Premarin at 1.25 mg three times a day. The conjunctiva taken from the eye at the second operation showed no difference in the ground substance of the blood vessels from those found in the first case. The second consisted of two cases in which 20 mg of estrogen was given intravenously, twelve and thirteen hours ahead of the operation. The third consisted of four cases in which conjugated estrogen was given in the dose of 20 mg one hour before the operation. Using Toluidin Blue and Colloidal Iron for stains it was not possible to demonstrate by ordinary histological means any difference in the ground substance of the specimen taken from the first eye and that from the second eye after conjugated estrogen.

It should be pointed out however that the dose given in these cases was the ordinary dose used in prophylaxis. A proportionate dose in an adult compared to the dose given by Schiff and Burn to their hamsters would require 50 to 60 mg of intravenous Premarin being used. Schiff and Burn also found that their time of maximum change was three hours after the administration of the conjugated estrogen.

#### DISCUSSION OF CLINICAL RESULTS

It should be noted from the series that while the incidence of secondary haemorrhage was greatly reduced as a result of the use of conjugated estrogen this dread complication was not completely abolished. However it is interesting to note that both those cases,

where secondary haemorrhage occurred, arose from injuries inflicted in the limbal area

Drs Brodin and Fox, in the Round Table discussion on haemostasis<sup>4</sup> noted that intravenous conjugated estrogen was beneficial in the treatment of oozing from an adenoid liver, but it was of much less value for a tonsil bed where ligatures were necessary. It therefore appears that intravenous use of conjugated estrogen is not likely to be so effective where the larger blood vessels of the ciliary body are torn, as in the trauma to the small vessels on the iris.

In the second article, written by the author, the idea was proposed that secondary haemorrhage possibly occurred in individuals where the body's own conjugated estrogen or physiological haemostatic agent was deficient. One of the reasons for believing this was that when a case had developed secondary haemorrhage after the original trauma, they frequently also developed secondary haemorrhage after any subsequent surgical intervention. Unfortunately, no test has yet been devised, at present, which can quickly determine whether there is any deficiency of the body's own estrogen level. It is possible that later we will be able to distinguish those cases which will develop secondary haemorrhage, from those cases which will not. When that day comes, it will be possible to administer a prophylactic dose of estrogen in a scientific manner and with the same confidence which we would have in treating any deficiency disease.

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# RADIOSULFATE RETENTION IN ORBITAL TISSUES RELATIONSHIP TO THYROTROPIC EXOPHTHALMOS \*†

HESEKEL M. HADDAD, MD ‡

The orbital tissues of the guinea pig and in particular the Harderian gland respond to thyrotropic hormone (TSH) administered to the animal by an increase in size. This induces proptosis<sup>1-6</sup>. In addition an augmentation of mucopolysaccharide synthesis<sup>6-8</sup> is suggested by the increase in the 24 hour uptake of radiosulfate<sup>7,10</sup>. The latter phenomenon offers a bioassay method for TSH like effect of sera of patients with endocrine exophthalmos. However for an adequate response an optimal dose of 1 unit of TSH per animal per day for two days is necessary.<sup>10</sup>

In the present study the sensitivity of the sulfate uptake of the Harderian gland in response to TSH is increased by using a 72 hour uptake (which will be called retention) instead of a 24 hour uptake. Using such a method the sera of 12 patients with endocrine exophthalmos are qualitatively assayed for TSH like effect.

## METHODS

Young female guinea pigs, in groups of 6 animals per experiment, were given carrier free  $S^{35}$ -labeled  $Na_2SO_4$ \* intraperitoneally. Thyrotropic hormone (TSH)† or serum in 0.5 ml saline solution was injected intraperitoneally simultaneously with the radiosulfate and daily thereafter for 2 days. Seventy-two hours after radiosulfate injection the animals were sacrificed. The orbital tissues and in particular the Harderian gland and the thyroid gland were dissected, cleaned of adventitia, weighed, hydrolyzed and counted individually in a Packard Tri-Carb liquid Scintillation counter.

The results (in counts/minute/mg of wet weight of tissue) were compared statistically using the  $t$  test (11). For this presentation,

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† Supported by Grant A-503, U.S. Public Health Service, National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda, Md. This study was presented at the International Congress of Ophthalmology in Delhi, India, December 27, 1962.

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\*  $S^{35}$ -labeled  $Na_2SO_4$  was purchased from Abbott Laboratories, Oak Ridge, Tennessee.

† TSH was used as the commercial preparation Thytropar, some purchased and some generously given by the Armour Laboratories.

however, the response of the tissue's radiosulfate was expressed as per cent of the control group for each experiment. Using percentage figures, a significant response was found to be roughly above a 12-15% increase in radiosulfate uptake.

### MATERIAL

Sera of 12 patients with endocrine exophthalmos (22-63 years old) were assayed using 0.1-0.2 ml of serum daily for 3 days per animal. The assay was made against a control group of animals injected with normal saline only, a group given TSH and a third group treated with sera obtained from euthyroid controls. For the latter purpose sera of 13 euthyroid controls (18-70 years old) were used individually or pooled.

Of the 12 patients, at the time of blood collection, 5 had inactive and 7 had progressive endocrine exophthalmos. Four of the patients were in hypothyroid state.

### RESULTS

**TSH EFFECT** Radiosulfate retention (72 hours uptake) by the Harderian gland of the guinea pig was highly responsive to TSH at as low a dose as 0.1 unit per day  $\times$  3. Even though there was considerable variation in the response from one experiment to the other, the increase in the Harderian gland's radioactivity ranged between 24 and 56% of the controls. The thyroid gland of the guinea pig responded significantly to TSH by an average increase in the radiosulfate retention by the gland of 34% of the control. A dose response curve is plotted on log-log coordinates (Fig. 1).

**SERUM EFFECT** Whereas there was very little variation in the response of the 72 hour radiosulfate retention by either the Harderian or the thyroid glands to different individual or pooled sera of euthyroid

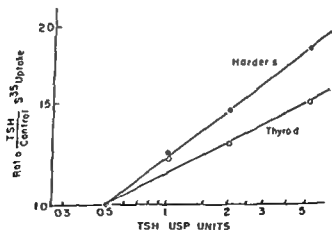


FIG. 1 Dose Response curve of TSH (in USP units) and the radiosulfate uptake by the Harderian and the thyroid glands (in fractions of normalized controls) plotted on log-log coordinates.

controls as compared to each other or to normal saline the sera of patients with endocrine exophthalmos behaved differently. Of the 7 patients with progressive exophthalmos (Table I) sera of 3 augmented the sulfation of the Harderian gland significantly (19-45%) and one serum showed no effect. Of the 5 patients with inactive exophthalmos on the other hand 2 sera caused no stimulation of Harderian gland sulfation 2 sera each induced 11% increase in the gland's radiosulfate and the fifth serum augmented sulfation significantly by 20% above the control.

The response of the thyroid gland of the guinea pig to the patients' sera did not follow specifically the activity or inactivity of the exophthalmos. Interestingly enough the response varied according to the thyroid status of the patient, namely whether the patient was euthyroid or hypothyroid. As seen in Table I there was significant augmentation of thyroid sulfation by the sera of the four patients who were hypothyroid, ranging between 15 and 41% of the control. Of the other 8 euthyroid patients there was an apparent diminution in the gland's radiosulfate induced by sera of 4 patients, whereas an insignificant increase (4-12%) was induced by the sera of the rest.

TABLE I

	Age Years	Sex	PBI mcg/100 ml	% deviation from control of $S^{35}$ uptake Harderian gland Thyroid gland	
				Harder	Thyroid
I Progressive Exophthalmos Euthyroid Status					
1 J L*	63	M	7.2	+27	-23
2 C K†	49	F	5.0	+45	+11
3 C McK	37	F	6.0	+0	-23
II Progressive Exophthalmos Hypothyroid Status					
4 H P*	42	F	4.1	+17	+15
5 E D	22	F	4.1	+27	+29
6 T D‡	62	M	3.3	+19	+16
7 J W	45	F	4.0	+37	+41
III Inactive Exophthalmos Euthyroid Status					
8 B R	36	F	8.1	+11	-14
9 M M	49	F	8.0	+11	+4
10 O S	58	M	6.1	-7	-8
11 F F	50	M	4.9	+20	+12
12 H W**	55	F	6.4	-1	+4

Unilateral exophthalmos both of the right eye

† The radiosulfate uptake by the Harderian gland increased from 21% to 45% above control within a period of 3 months during which her exophthalmos became remarkably worse.

Exophthalmos developed almost simultaneously with thyrotoxicosis. Patient was decompressed unilaterally; biopsy was read as pseudotumor. Exophthalmos responded to steroid therapy.

\* Exophthalmos regressed



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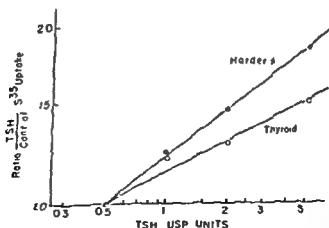


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## DISCUSSION

The stimulating effect of TSH on the Harderian gland of the guinea pig was found to increase the 24 hour radiosulfate uptake by this gland but only in doses of 1 unit per day for 2 days (10). In order to devise a bioassay method for TSH-like effect based on such response, the sensitivity of the response had to be increased several folds. Direct tissue paper chromatograms demonstrated that a large percentage of the radiosulfate in the gland at 24 hours remained in its inorganic form. The possibility that the increase in the gland's radiosulfate in response to TSH was mainly in the organic sulfate fraction was recently corroborated by Brumsh (12). Since our study depends practically on direct tissue assay of radioactivity, the elimination of the inorganic radiosulfate fraction by dialysis or other physical means would be impractical. Using direct tissue chromatography as an index, however, it was found that by allowing the administered radiosulfate to remain in the animal about one biological half life (about 72 hours) prior to killing, almost all the inorganic radiosulfate fraction in the Harderian gland disappeared. Thus the method of study was modified from a 24 hour uptake to a 72 hour "retention" of radiosulfate by the Harderian gland of the guinea pig.

The response of both the Harderian and the thyroid glands to TSH were improved several folds using a 72 hour uptake of radiosulfate. As seen in Fig. 1 this response had the potentiality for a bioassay method for TSH like effect.

The response of the Harderian gland to the sera of patients with endocrine exophthalmos demonstrated the utility of this response as at least a qualitative bioassay method.

The response of the thyroid gland of the guinea pig to the sera of patients with endocrine exophthalmos correlated with the clinical (hypothyroidism and myxedema), and biochemical (serum PBI and cholesterol) status. This pointed to a dissociation in the response of the two tissues of the guinea pig to patients sera versus TSH. It further suggested that commercial TSH had an additional factor which stimulated the orbital tissues of the guinea pig as has already been pointed out by other observers (13-14). But most important was the suggestion that a humoral factor existed in patients with endocrine exophthalmos which stimulated only the orbital tissue of the guinea pig even when no evidence for increased circulating TSH was elicited. The nature of this factor is yet to be determined. It may, however, be assayed qualitatively at least, using the Harderian glands 72 hour retention of radiosulfate as an index. Quantitative bioassay would remain difficult until the exact nature of this factor and its actual influence on guinea pig orbital tissue are determined unequivocally.

## SUMMARY

Using 72 hour radiosulfate uptake (retention) the Harderian and the thyroid glands of the guinea pig responded to as little as 0.1 unit of TSH per day administered for three days to the animal. Using this response as an index sera of 12 patients

with endocrine exophthalmos were assayed. Sera of 6 out of 7 of the patients with progressive exophthalmos induced significant increases in the Harderian radiosulfate whereas the serum of only one out of 5 of the patients with inactive exophthalmos caused a similar response. The response of the thyroid gland to these sera indicated a dissociation in the response of the two tissues since the thyroid response depended on the titer of circulating TSH as evidenced by clinical and biochemical criteria.

#### ACKNOWLEDGEMENT

The author expresses his thanks to Mr Raymond Grant and Miss Aleene Schneider for their expert technical assistance and to Dr Bernard Becker for his help and suggestions.

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Using 72 hour radiosulfate uptake (retention) the Harderian and the thyroid glands of the guinea pig responded to as little as 0.1 unit of TSH per day administered for three days to the animal. Using this response as an index sera of 12 patients

be treated, and finally a stage where certain types of cases are treated even although degenerative changes are absent or invisible

The following have reported on the treatment of retinal holes Sabbadini (1934) Amsler (1938), Fleischer (1947) Weber (1947), Franceschetti and Balavome (1949), Custodis (1950), Sedan Bauby (1950) Schepens (1950 1952), Safar (1953), Meyer Schwickerath (1956) Amiga (1958), Berliner (1958) Arruga (1958) Dollfuss (1958), Schepens (1958) Shapland (1958), Callahan (1958) Hruby (1958), Jess (1958), Amsler (1959) Bietti (1959), Schiff Wertheimer and Paufigue (1959), Safar (1959) Franceschetti and Maeder (1959), Lindner (1959) Meyer Schwickerath (1959), Pischel (1959), Weve (1959) Lincoff (1961) These authors differ among themselves with regards to insistence on which holes to close Among the more conservative are Berliner Bietti Dollfuss, Safar Schiff Wertheimer and Paufigue, and Schepens The following factors were by most authors considered decisive The age of the hole and its tendency to heal its size form and position whether single or multiple the presence of vitreous attachment in the neighbourhood, the refraction of the eye, the presence of a history of detachment in the fellow eye the age temperament and occupation of the patient and a family history of detachment Complaints of flashes are usually significant

The treatment of degenerative areas has been described by Weber (1947) Franceschetti (1955) Arruga (1958), Dollfuss (1958) Callahan (1958) Jess (1958) Amsler (1959) Lindner (1959), Sabbadini (1959), Schiff Wertheimer and Paufigue (1959) Maeder (1959), Meyer Schwickerath (1959) (1515 cases) Pischel (1959) Weve (1959), Custodis (1960) (757 cases) and Lincoff (1961) Factors to be considered before deciding on treatment for degenerative areas are their extent situation and progressive nature, their presence in second eyes the imminence of cataract extraction especially in myopia the youth of the patient and complaints of flashes Most surgeons are conservative regarding the treatment of degenerative areas and confine themselves to those where there is vitreous pull Heinzen (1960) divides the changes which may require treatment into five groups Pigment verschiebung, cobblestones rosettes palliades and nail tracks

There is finally the group of cases in which prophylactic treatment is frequently carried out even in the absence or near absence of degeneration These include cataract extraction in second eyes, in high myopia, or in cases such as Marfan's syndrome, where there is a danger of vitreous loss (Schiff Wertheimer 1958 Mylius 1959 Paufigue and Spira 1959 Klotz, 1961 Lincoff 1961)

Heinzen (1960) in discussing the need for preventive measures compares the risk of photocoagulation (1% out of 1 000 treated cases developed retinal detachment in the series reported by Meyer Schwickerath 1959) with the probability of detachment occurring after spontaneous hole formation Regarding this latter probability, there is much difference of opinion Colyear and Pischel (1956) found that detachment followed in 20% of retinal holes On the other hand

## A NATIONAL COOPERATIVE STUDY IN THE PREVENTION OF RETINAL DETACHMENT—A PRELIMINARY REPORT

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(Co ordinators)

W. Felsenthal, I. Hauer, M. Ivry, G. Kallner, O. Kurz, R. Sachs,  
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Although there is now a high possibility of successfully treating a detachment of the retina, failures in most clinics are still between 20-30% and in the best of cases there are months of cumbersome invalidity. Preventive measures are, therefore, important and the purpose of this communication is to assess the effectiveness of this as shown in a national cooperative study being carried out in Israel since 1960.

Prophylactic treatment of detachment of the retina consists of therapy applied to a retinal lesion before there is actual detachment. Included in these lesions are retinal tears where the lid only is lifted into the vitreous.

The possibility of preventive treatment of retinal detachment is based on three circumstances:

- (a) In the majority of cases of idiopathic retinal detachment the detachment retinopathy goes through a phase of predetachment changes.
- (b) Photocoagulation by means of the apparatus designed by Meyer Schwickerath provides a relatively easy and safe alternative to diathermy in the treatment of the predetachment phase, although in many cases diathermy is the more suitable method.
- (c) Refined methods of ophthalmoscopy make it possible to visualise with ease the fundal changes in the pre detachment phase.

Theoretically it is possible to prevent the majority of retinal detachments by means of the discovery and treatment of the predetachment phase in all potential cases.

The history of the prophylactic treatment of retinal detachment can be divided into three stages. A stage where the prophylaxis was confined to retinal holes and involved a discussion as to which holes should be closed, a later stage, where prophylaxis extended to the treatment of the pre hole retinal degenerative changes and included discussion of the circumstances under which certain changes should

(A) The factors initiating the degenerative stage are situated presumably in either the choriocapillaris or in the vitreous, or in both simultaneously. There is histological evidence for each of these factors. Okun has shown that obliteration of the choriocapillaris may be associated with cystoid degeneration and pigment loss. On the other hand vitreo retinal adhesions seem capable of giving rise to cystoid changes and disturbances in the retina (Fig 1 and 2). It has been suggested that the pull of a vitreous adhesion gives rise to cystoid changes and thereafter the continuation of the pull converts the cystoid change into a hole. The histological findings in a case previously reported to the Congress suggest that changes in the choriocapillaris and vitreous may contemporarily produce the retinal degenerative changes. It is not likely that clinical observations will finally determine the nature of the initiating factor except in a small minority of cases. The clinical presence of vitreous pull does not obviate the possibility of an initiating choroidal factor and the clinical absence of vitreous pull does not prove that it was not at one time present (Fig 3). The evidence regarding the nature of the initiating factor will then probably be microscopic rather than clinical in nature and therefore is not likely to accrue from the clinical studies which are the subject of this report.

(B) On the other hand the temporal relationship of the details of the degenerative stage may well be studied clinically and the relationship of pigment proliferation, cystoid degeneration, snail tracks, pallisade formation and vascular sclerosis be determined. The role of the vitreous pull in a final factor in the hole formation is accepted, but there is not yet commonly accepted evidence regarding the type of retinal degeneration which is ominous of hole formation, and if so to which type of hole or whether indeed retinal degeneration must always be clinically present.

(C) Finally it should be possible to determine by planned clinical study which type of hole most frequently gives rise to detachment and the time it may take to do so.

The problems may be stated tabularly as follows —

(A) Initiating Sequence	(B) Degeneration hole Sequence	(C) Hole-detachment Sequence	
Vitreous Pull or Choriocapillaris Occlusion or both	Pigmentation Cystoid— Degeneration Snail tracks Lattice— Formation Vascular— Sclerosis	Circular Hole  Horse shoe hole	Retinal Detachment  No Retinal Detachment



Adams (1956), Teng and Chi (1957), and Okun (1961), found the occurrence of holes in so called normal eyes far beyond what the incidence of retinal detachment might lead to expect. There is, as can be easily understood, even greater unpredictability of prognosis in many types of retinal degeneration with regards to the likelihood of a supervening hole formation.

There are three main problems in the preventive treatment of retinal detachment, all of which have in only a certain measure been solved by the authors whose works have been quoted.

- (a) How can eyes with pre detachment changes be discovered. Some cases, probably most, have symptoms of muscle or flashes at one time or another, yet there are many cases where those are slight or do not drive the patient to the oculist, or their implication not appreciated by the examiner.
- (b) How can it be statistically proved that retinal detachment has been prevented by prophylactic measures.
- (c) What is the natural history of the pre detachment phase. What retinal, choroidal or vitreal changes or combination of changes proceed to hole formation, and which holes lead to retinal detachment.

#### REQUIREMENTS AND POSSIBILITIES

The discovery, in large numbers, of cases with pre detachment retinopathy is dependent on the setting up of special retinal clinics in each department where patients with symptoms suggestive of the retinopathy may be examined by ophthalmoscopists specially experienced in the necessary techniques and with plenty of time to do so. In addition groups of cases have to be specially invited and examined in which the expected incidence of retinal detachment is relatively high. As will be seen later the invited groups in Israel are "second eyes" and "aphakic myopes".

Statistical proof of the efficacy of preventive measures depends on the consideration of the incidence of retinal detachment throughout a confined geographical area during a number of years and the effect on this incidence of a known number of prophylactic measures. In this way it will be possible to determine if expected incidence has been diminished as the result of stated preventive measures. It will not be possible to answer this problem if patients go to different ophthalmologists for diagnosis, preventive measures or perhaps a subsequent detachment and these ophthalmologists are not in a position to pool their findings. Briefly, the statistical proof of the efficacy of preventive measures depends on these measures and the incidence of detachment being made notifiable.

The pre detachment phase of detachment retinopathy which may be present for years may be subdivided as follows:

- (A) Initiating Sequence
- (B) Degeneration hole Sequence
- (C) Hole Detachment Sequence

We are of course interested in the types of patients with a certain predominance in retinal detachment whose population (being the population at risk') is low in the general population, and who are likely to be in attendance at an ophthalmic department

With these considerations in mind the following types of patients are being especially examined for the presence of pre detachment retinopathy

- (1) The 'second eye' in all cases of retinal detachment
- (2) All cases of aphakia with myopia
- (3) All cases presenting symptoms suggestive of detachment retinopathy

In most of the departments involved in this study, special clinics have been set up for the investigation of these types of patients. These departments are prevention detachment minded and have photocoagulation equipment at their service

#### B TO PROVE THAT RETINAL DETACHMENT HAS BEEN PREVENTED

Preventive retinal detachment may be said to have been begun on an intensive scale in Israel in January 1960. The rate of incidence of retinal detachment per 100 000 of the population over 40 years of age in the four years (1956-1959) is shown in Fig. 4 and will be compared with that of the ten succeeding years (1960-1969). Special reference will be made to the incidence among second eyes and aphakic myopes. In addition note is made of all cases of preventive therapy carried out since 1960 and an association sought between the number of these cases and any change that may be noted in the incidence of retinal detachment during the 1961-1969 period. During the 1960-69 period the following data from each department will be received

- (a) The total number of eyes operated on for retinal detachment
- (b) The number of second eyes in the total number of eyes operated on for retinal detachment
- (c) The number of aphakic myopic eyes in the total number of eyes operated on for retinal detachment
- (d) The number of preventively treated eyes
- (e) The number of second eyes treated preventively
- (f) The number of aphakic myopic eyes treated preventively

#### C TO DETERMINE THE NATURAL HISTORY OF THE PRE DETACHMENT PHASE OF RETINAL DETACHMENT

To achieve this as many as possible cases of suspected detachment retinopathy in the pre-detachment phase have completed with respect to them an investigation sheet which is common to all the departments in the country (Fig. 5). In this sheet are noted data regarding history, symptomatology and ophthalmoscopic changes

The problems implicit in A (initiating sequence) probably depend for their solution on histological studies, while those of B and C (degeneration hole sequence and hole detachment sequence) may well be clarified by an organised large scale clinical study which is now being described

In order to attempt to answer these questions of clinical pattern and those of proof of the efficacy of preventive measures, the 7 main ophthalmic departments in Israel have been combined in a cooperative study. These departments have a total of 207 beds. Quarterly statistics of preventive measures, and detachment incidence are centralised for review. In addition a common case history sheet is used, the facts on which are periodically transferred to a central system of marginal punch cards. Between 1956 and 1959 (preventive therapy may be considered to have begun in 1960), about 180 retinal detachment eyes were treated each year. The purpose of this communication is to describe the methods used in this study and to give a preliminary report on the results achieved and expected.

## METHODS AND MATERIAL

### A THE DISCOVERY AND TREATMENT OF EYES WITH PRE DETACHMENT CHANGES

As already stated, patients with pre detachment changes either come to the doctor with complaints of *muscae* or *flashes*, or, having little or no symptoms, must be sought out and brought to examination. Concerning the latter, there are certain types of individuals that are liable to retinal detachment. The following table lists the main types of patients found in retinal detachment cases, their percentage incidence as noted in published reports, their percentage incidence in cases occurring in Israel between 1956 and 1959, and the estimated number of patients of each type at risk in Israel in 1960.

Types of Individuals	Average % Incidence of types in cases of Detachment reported in World literature	Average % Incidence of types in cases of Detachment in Israel 1956-1959	Number of Cases at risk in Israel in 1960
Myopia less than 5 D	25 %	30 %	about 95 000
Myopia 5 D or over	37 %	40 %	about 95 000
Aphakia	10 %	11 %	7 000    000
Myopia and Aphakia	7 %	8 %	1 000
Second Eyes *	20 %	12 %	1 000

## **SUR L'IMPORTANCE DE LA DEFECTOSCOPIE ULTRASONIQUE DANS L'OPHTALMOLOGIE**

**JAN VANYSEK ET JULIANA PREISOVA**

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Notre travail préliminaire sur l'utilisation d'un examen apparemment simple de l'œil humain par un defectoscope ultrasonique a impulsions introduit dans l'ophtalmologie par Mundt et Hughes (1) et qui a été élaboré depuis 1957 surtout par Oksala (2-17) a montré que cette méthode bien que certainement de valeur, n'a pas une valeur unique de preuve.

L'interprétation des courbes dans les échogrammes des tissus normaux et pathologiques intra-oculaires paraît souvent contestable. Quelques échos, désignés comme reflet surtout de corps étrangers à l'intérieur de l'œil pour la plupart pas contrastants par rayons X n'ont jusqu'à présent pas cette possibilité de preuves demandée par le clinicien à une telle méthode. Cette imperfection des résultats de Oksala et aussi des nôtres a conduit à un certain scepticisme que l'on trouve aussi dans le travail de Baum et de Greenwood (18). Ces derniers auteurs ont en 1961 apprécié à leur juste valeur 16 travaux de Oksala et son interprétation des échogrammes pathologiques. Baum et Greenwood ont certes employé des appareils provenant d'une autre usine que ceux d'Oksala mais ils ont travaillé avec des sondes de la même fréquence dans des conditions à peu près parallèles. Ils considéraient les résultats d'Oksala comme contestables.

À notre clinique nous travaillons depuis plus de deux ans avec la defectoscopie ultrasonique. Nous avons déjà publié nos premiers résultats (19). Les principaux devoirs que nous nous sommes posés dans notre travail étaient la mesure de plusieurs distances dans l'œil c'est à dire la mensuration de la profondeur de la chambre antérieure et de l'axe optique de l'œil, puis le diagnostic par rayons X de corps étrangers non contrastants et dans les derniers temps surtout le diagnostic différentiel de décollements simples et secondaires de la rétine.

### **METHODOLOGIQUE**

Les examens ont été effectués au moyen d'un defectoscope ultrasonique de la firme Kretz 1000 M avec une sonde de barium — titanate d'une fréquence de 6 MHz d'un diamètre appliqué de 6 mm. Au cours de ces examens nous avons trouvé que la meilleure méthode était de travailler avec l'impulsion 2 et le renforcement 10. Si nous avons employé une autre impulsion ou une sonde d'une autre fréquence

which may be relative to the case. Information regarding any preventive measures carried out is noted. Details regarding the state of the vitreous and changes in the fundus, including pigmentation, choroidal changes, lattice formation, cystoid degeneration and hole formation, are so arranged, that they can be transferred to marginal punch cards. Periodically these case sheets are centralised into a central office, where any new information is transferred to the punch card record. The case sheets are then returned to the various departments. The information on the punch cards will be analysed with respect to the problems of the natural history of the pre detachment phase already detailed.

## RESULTS

Despite the 369 eyes that have been preventively treated since 1960, there is no change in the incidence of retinal detachment in the population during the years 1960, 1961 and 1962, the necessary corrections having been made for increase and ageing of the population. This may mean either that only a small percentage of the eyes treated would, if untreated, have developed retinal detachment, or that the latency between hole discovery and detachment formation is longer than the period under observation. Two out of the 5 cases with retinal hole, which ultimately developed detachment, observed by Colyear and Pischel (1956), did so after 1 year and 2 years and 9 months respectively. It is obvious that further observation over a number of years will be required in order to indicate the extent to which the incidence of retinal detachment may be affected by means of preventive measures.

Besides the unknown, but probably years long latency between hole formation and retinal detachment, there are other, chiefly organisational factors, which indicate that the expected fall in incidence will gather momentum after a few years. The retinal clinics are being more organised to deal with the patient who, because of symptoms or because he falls within the group of second eyes or myopic aphakics, is a candidate for detachment, and the general ophthalmologist is becoming more aware of the possibilities of preventive therapy.

If we assume a straight line from the pre test period average of 27.6 p 100,000 to half that number (13.8 p 100,000) during 10 years the rate should, after 5 years be at 75% of the original, at 20.7. In view of the fact that — as experience of the first years of the test period has shown — it will take some years until the preventive observation programme will be in full operation, we will assume arbitrarily that after 5 years only 85% rather than the level of 75% will be reached. This would give us the rate of (85% of 27.7 =) 23.5 for the year 1964.

The period of observation is too short to permit definitive observations regarding the evolution of the pre detachment phase of retinal detachment. The method of a national cooperative study seems, however, to be a valid one for answering the problems posed, and it is hoped that it may be possible to contribute to their solution in further reports.

1 F S 42 ans, num 174/62 Dans l'anamnèse il voyait un rond devant l'oeil droit pendant deux mois

VOD 6/60 sl + 2 0 comb + 1 II cyl axe 90°  
6/36

VOS 6/15 + 2 0 comb + 1,5 axe cyl 120°  
6/15

Sur le fond de l'oeil droit il y a nasalement et temporalement de la papille un relèvement sphérique de la rétine avec des signes caractéristiques d'une croissance de tumeur La tension intraoculaire est de 24 mm/Hg Par la lampe de Lange par voie non operative la malformation n'était pas accessible L'épreuve du mélanin dans l'urine dans un des examens était positive

L'examen ultrasonique de l'oeil droit de nombreux échos pathologiques d'après l'emplacement de la sonde, prouvent les reflets d'une malformation massive La localisation est conforme à l'examen ophtal



FIG 1 Echogramme numero 1303  
Malade F S numero d'observation 174/62 Diagnostic Melanoblastome choroïdica oc dr La sonde a été appliquée dans le méridien de 12 h à une distance de 3 mm du limbe

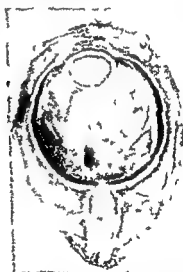


FIG 2 Le même malade Coupe longitudinale du bulbe encléé montrant la tumeur d'une grandeur de 7 x 8 mm dans le quadrant supéro-temporal.

mologique (Fig 1) Au cours de l'examen macroscopique du bulbe encléé nous avons constaté un melanoblastome de la choroïde à l'endroit décrit c'est à dire dans le quadrant supéro-temporal pres du pôle postérieur une malformation typique de la forme d'un champignon grisâtre blanchâtre d'une grandeur de 7 x 8 mm (Fig 2)

nous citons ce fait toujours au cours de l'examen même. Ce n'est que depuis deux mois que nous pouvons employer le dernier appareil Kretz 7000, approprié spécialement à l'emploi médical, tandis que l'appareil précédent avait été construit surtout pour la métallurgie. En attendant il nous est impossible de comparer les résultats obtenus avec les deux appareils. Mais on peut dire préliminairement que l'appareil Kretz 7000 aura beaucoup d'avantages. Nous avons effectué l'anesthésie de l'œil avec 5% de cocaïne. Comme moyen de liaison nous avons employé de la paraffine liquide. Nous avons enregistré toutes les constatations par photographie. Nous avons appliqué la sonde tantôt dans le centre de la cornée, tantôt sur le limbe dans le méridien 3, 6, 9 et 12 h et plus, sur la sclérotique à une distance de 6 à 8 mm du limbe dans les mêmes méridiens. Nous avons toujours tâché d'appliquer la sonde de façon à ce que l'axe des rayons ultrasoniques passe du moins approximativement par le centre du bulbe. Chez tous les malades nous avons aussi examiné l'autre œil.

Mise au point des résultats. Jusqu'à présent nous avons fait environ 1700 photographies d'échogrammes ce qui correspond à un double nombre d'examen effectués. Tous les cas de caractère banal ou répétés avec le même résultat n'ont pas été photographiés. Dans notre première communication nous avons cité positivement les possibilités de localisation de corps étrangers dans l'œil intérieur par l'ultrason. Dans ce groupe provisoire notre matériel n'est ni assez étendu, ni assez édifiant pour pouvoir dès aujourd'hui essayer de donner une appréciation à sa juste valeur. La localisation de corps étrangers dans l'intérieur de l'œil par la defectoscopie ultrasonique doit en attendant être considérée comme méthode moins fiable et qu'il faut encore élaborer, c'est le cas pour beaucoup d'échos subordonnés causés par une hémorragie, une exsudation, une prolifération du tissu et par d'autres malformations pathologiques reflétant l'ultrason et à cause d'une assez grande zone morte de la sonde employée. Malgré que nous ne soyons pas sceptiques nous voulons ne pas faire d'erreurs provenant d'expériences peu étendues et insuffisantes.

Dans cette communication nous voulons faire part de 3 groupes d'examen, ce sont :

- A Les malades du décollement de la rétine cachant une tumeur intraoculaire
- B Les malades avec un décollement primaire de la rétine
- C Les personnes examinées avec défaut réfractaire ou la defectoscopie ultrasonique devait déterminer la longueur de l'axe optique de l'œil

Dans le premier groupe des malades avec un décollement de la rétine cachant une tumeur intraoculaire, nous avons choisi 10 malades ou après l'enucléation de l'œil il est possible de confronter le diagnostic ophtalmologique et les examen auxiliaires avec les examen ultrasoniques et histologiques. Nous donnons le compte rendu de ses malades en résumé :

## 3 A J, 55 ans, numero 1269/62

Dans l'anamnèse perception visuelle abolie de l'oeil gauche pendant près de deux mois. Suspecte d'un décollement primaire elle a été soignée dans un autre hôpital et seulement trois semaines après elle a été envoyée à notre clinique.

VOD mouvement, projection juste

VOS 6/8 + 0,5 D 6/6

Sur la rétine de l'oeil droit il y avait deux décollements sphériques sans déchirures dont l'un couvrait la moitié nasale entière le deuxième le quadrant inféro temporal. Le mélanin dans l'urine était faiblement positif par l'examen avec la lampe de Lange nous avons constaté dans la moitié nasale un assombrissement important. L'examen ultrasonique a donné deux sortes de constatations. Dans plusieurs projections nous avons constaté isolément un écho pathologique correspondant au sommet de la rétine décollée.

En appliquant la onde à VI h à 10 mm du limbe nous avons vers la fin de l'échogramme eu de nombreux échos pathologiques témoignant pour une malformation solide. Après l'encléation du bulbe nous avons constaté un mélanoblastome spinocellulaire localisé sous la région centrale d'une grandeur de 12 × 6 mm.

## 4 A S 59 ans numero 1278/62

Dans l'anamnèse vision d'un fil devant l'oeil droit pendant 5 mois.

VOD 4 m doigts

VOS 6/12

À l'oeil droit nous avons constaté un décollement de la rétine de V à VII h qui avait toutes les marques d'un décollement primaire sans déchirure. De VII à IX h il y avait un décollement gris de caractère plutôt sphérique se terminant abruptement. L'examen avec la lampe de Lange montre un assombrissement vers VII h. L'épreuve du mélanin dans l'urine était négative. La tension intraoculaire était de 24 mm Hg. L'examen ultrasonique a montré un type d'échogrammes démontrant un simple décollement et un autre type démontrant par de nombreux échos une tumeur selon l'application de la sonde. L'application de la sonde était particulièrement démonstrative contre l'endroit de la tumeur suspecte (Fig 5), et au dessus de la tumeur (Fig 6) ou les échos typiques étaient soit à la fin soit au commencement de l'échogramme. Après l'encléation nous avons constaté dans le quadrant inféro-temporal de l'oeil droit immédiatement derrière l'équateur un mélanoblastome de la forme d'un champignon d'une grandeur de 6 × 7 mm (Fig 7).

## 5 V J 60 ans numero 1222/62

Dans l'anamnèse le malade a signalé que trois jours avant sa venue à l'hôpital il a senti de grandes douleurs à l'oeil gauche et qu'il a



2 C J, 46 ans, numero 262/62 Dans l'anamnese il y a 1 mois blesse à l'oeil gauche d'une contusion par une pierre. À présent il voit mal de cet oeil depuis 2 mois. Dans un autre hopital il a été soigné conservativement d'un décollement primaire de la rétine. Après insucces de la therapie il a été envoyé à notre clinique pour être examiné.

VOD 5/5

VOS 1 m doigts

À l'oeil gauche, décollement gris de la rétine abruptement limité vers la papille, plus plat vers la périphérie. Sur le décollement pigmentation isolée. La lampe de Lange brille partout, tension intra oculaire 15 mm/Hg.

*Examen ultrasonique* l'application de la sonde, à l'IN h sur le limbe a montré de nombreux echos pathologiques, temoignant du



FIG 3 Echogramme numéro 1329 Malade C J numero d'observation 262/62 Diagnostic Melanoblastome choroïdéal oc. sin. La sonde a été appliquée dans le méridien de l'IN h à une distance de 5 mm derrière le limbe.



FIG 4 Le même malade. Coupe longitudinale du bulbe enclévé montrant la tumeur d'une grandeur de 6 x 11 mm dans la moitié temporale du bulbe atteignant la région centrale.

reflet d'une matière massive devant la fin du bulbe (Fig 3). Après l'enclévation, après l'ouverture du bulbe fixe, nous avons constaté un melanoblastome dans la région centrale de l'oeil gauche, surtout dans la moitié temporale, d'une grandeur de 6 x 11 mm, la rétine au dessus était décollée (Fig 4).

## 3 A J 55 ans numero 1269/62

Dans l'anamnèse perception visuelle abolie de l'oeil gauche pendant près de deux mois. Suspecte d'un décollement primaire elle n'a été soignée dans un autre hôpital et seulement trois semaines après, elle a été envoyée à notre clinique.

VOD : mouvement, projection juste

VOS 6/8 + 0.5 D 6/6

Sur la rétine de l'oeil droit il y avait deux décollements sphériques sans déchirures dont l'un couvrait la moitié nasale entière le deuxième le quadrant inféro temporal. Le mélanin dans l'urine était faiblement positif, par l'examen avec la lampe de Lange nous avons constaté dans la moitié nasale un assombrissement important. L'examen ultrasonique a donné deux sortes de constatations. Dans plusieurs projections nous avons constaté isolément un écho pathologique correspondant au sommet de la rétine décollée.

En appliquant la sonde à XI h, à 10 mm du limbe nous avons vers la fin de l'échogramme eu de nombreux échos pathologiques témoignant pour une malformation solide. Après l'enucléation du bulbe nous avons constaté un melanoblastome spinocellulaire, localisé sous la région centrale d'une grandeur de  $12 \times 6$  mm.

## 4 A S, 59 ans numero 1278/62

Dans l'anamnèse vision d'un fil devant l'oeil droit pendant 5 mois.

VOD 4 m doigts

VOS 6/12

À l'oeil droit nous avons constaté un décollement de la rétine de V à VII h qui avait toutes les marques d'un décollement primaire sans déchirure. De VII à IX h il y avait un décollement gris de caractère plutôt sphérique se terminant abruptement. L'examen avec la lampe de Lange montre un assombrissement vers VII h. L'épreuve du mélanin dans l'urine était négative. La tension intraoculaire était de 24 mm Hg. L'examen ultrasonique a montré un type d'échogrammes démontrant un simple décollement et un autre type démontrant par de nombreux échos une tumeur selon l'application de la sonde. L'application de la sonde était particulièrement démonstrative contre l'endroit de la tumeur suspecte (Fig 5), et au dessus de la tumeur (Fig 6) où les échos typiques étaient soit à la fin soit au commencement de l'échogramme. Après l'enucléation nous avons constaté dans le quadrant inféro-temporal de l'oeil droit immédiatement derrière l'équateur un melanoblastome de la forme d'un champignon d'une grandeur de  $6 \times 7$  mm (Fig 7).

## 5 V J 60 ans numero 1222/62

Dans l'anamnèse le malade a signalé que trois jours avant sa venue à l'hôpital il a senti de grandes douleurs à l'oeil gauche et qu'il a



FIG 5 Echogramme numero 1583 La malade A S numéro d'observation 1278/62 Diagnostic Melanoblastome choroïdéal oc dx La sonde a été appliquée dans le méridien de II h à une distance de 6 mm du limbe directement contre la tumeur

FIG 6 Echogramme numero 1587 La même malade La sonde a été appliquée au-dessus de la tumeur dans le méridien de VII h à une distance de 10 mm du limbe



FIG 7 La même malade Coupe longitudinale du bulbe enclavé montrant la tumeur dans le quadrant inferotemporal d'une grandeur de 6 x 7 mm

tout d'un coup cessé de voir. Après 2 jours dans un autre hôpital il a été envoyé à notre clinique.

VOD 6/6

VOS 0

À l'œil gauche les deux paupières et aussi la peau du côté gauche de la joue étaient œdémateuses. La mobilité du bulbe vers le bas et vers la tempe était limitée. La conjonctive bulbaire chemotique dans la moitié inférieure du bulbe prolabaient au dehors entre les paupières. La cornée était grisâtre, de surface finement bosselée hyperhémique de l'iris. Le réflexe rouge était inexistant. Le bulbe en protrusion de deux mm. Après une thérapie conservatrice anti-inflammatoire et contre glaucomateuse il a été possible de voir un profond décollement sphérique de la rétine gris-vert de V à X h couvrant la papille. La tension intraoculaire était de 62 à 42 mm/Hg. L'examen avec la lampe de Lange a montré un assombrissement entre IV à VI h. L'examen ultrasonique a montré à l'application de la sonde sur le limbe à IX h plusieurs échos pathologiques placés étroitement l'un à côté de l'autre comme reflets d'une malformation massive. Après l'énucléation nous avons constaté vers le pôle postérieur une tumeur plate d'une hauteur de 5 mm d'une longueur de 17 mm.

6 J. K. 63 ans numéro 1270/62

Dans l'anamnèse elle a observé durant les deux derniers mois une perception visuelle amoindrie de l'œil droit.

VOD 2 mètres et demi doigts

VOS 6/10 sl

À l'œil droit la rétine était décollée dans le quadrant inféro-nasal et dans toute la moitié temporale. Entre IX et I h, elle était à la périphérie gris foncé, autre part gris clair. La tension intraoculaire était de 25 mm/Hg. L'examen avec la lampe de Lange démontrait un faible assombrissement entre X et I h à une distance de 10 mm du limbe. L'examen ultrasonique a démontré des échos pathologiques presque dans tous les méridiens. Du côté nasal nous avons constaté un type d'échos témoignant d'un simple décollement de la rétine dans le quadrant inféro-temporal et un type de nombreux échos témoignant d'une malformation massive devant la paroi postérieure du bulbe. À l'application de la sonde contre la tumeur suspecte (Fig. 8).

Après l'énucléation du bulbe nous avons constaté un mélanoblastome s'étendant depuis la racine de l'iris jusqu'au pôle postérieur presque sur toute la moitié postérieure du bulbe, plutôt vers le quadrant supéro-temporal. Il était plat d'une hauteur de 4 à 5 mm (Fig. 9).

7 F. J. 77 ans numéro 416 62

Dans l'anamnèse elle a été traitée depuis sa soixantième année d'une anémie pernicieuse.

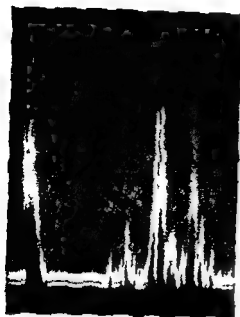


FIG 8 Echogramme numero 1559  
La malade J. K. numero d'observation 12/0/62 Diagnostic Melanoblastoma choroïdère oc de La sonde a été appliquée contre la tumeur dans le méridien de 11 h sur le limbe



FIG 9 La même malade Coupe longitudinale du bulbe encléé montrant la tumeur d'une hauteur de 4 mm remplissant presque toute la moitié postérieure du bulbe

Une semaine auparavant la malade a ressenti des douleurs à l'œil droit et celui-ci était rouge

VOD projection lumineuse déficiente

VOS 6/12 sl + 2,00 D 6/6 sl

La peau de la paupière inférieure et de la moitié supérieure de la joue droite était rouge, tout la conjonctive bulbaire était chemoïque Sur le fond, un décollement hâtif de la rétine avec trois ballons de II à V h, de V à VIII h et de VIII à XI h,

L'examen avec la lampe de Lunge la pupille ne brillait pas de XII à X h

La tension intraoculaire était de 15 mm/Hg

L'examen ultrasonique a démontré des échos typiques, nombreux, placés très densément l'un à côté de l'autre, très très bruts et cela surtout sur l'échogramme entier à l'application de la sonde à 12 h (Fig 10) Après l'enucléation on a trouvé dans le corps ciliaire et dans la choroïde, dans le quadrant inféro-temporal, un mélanoblastome de 14 x 9 mm, la rétine devant lui était décollée (Fig 11)

8 M D, 58 ans, numero 1012/62

Dans l'anamnèse perception visuelle amoindrie de l'œil droit pendant 4 mois Pendant ce temps la malade a été traitée dans l'ambu



FIG. 10 Echogramme numéro 136°  
La malade F J numéro d'observation 41662 Diagnostic Melanoblastoma corporis ciliaris et chorioideae oc dx La sonde a été appliquée dans le méridien d'1 h à 3 mm derrière le limbe au dessus de la tumeur



FIG. 11 La même malade Coupe longitudinale du bulbe encléé montrant la tumeur dans le quadrant inferotemporal d'une grandeur de 14 x 9 mm

lance par le médecin du secteur, d'une tension intraoculaire augmentée bilatérale 4 jours auparavant la malade a eu une attaque glaucomateuse de l'œil droit

VOD projection de lumière seulement temporale

VOS 62 + 15 D 66

Les deux paupières de l'œil droit étaient énormément enflées la conjonctive bulbaire était chemotique La corneée grisâtre finement bosselée l'iris congestionnée La lentille était diffusément troublée A l'examen avec la lampe de Lange nous avons constaté que dans la moitié temporale la pupille ne brillait pas La tension intraoculaire originale 49 mm Hg a été normalisée par un traitement conservatif à 15 mm Hg L'examen ultrasonique a démontré de nombreux échos pathologiques typiques pas trop hauts et placés très près l'un de l'autre échos d'une malformation massive et cela à l'application de la sonde d'une part contre la moitié temporale du bulbe dans les deux tiers de l'échogramme postérieur (Fig 12) et au commencement de l'échogramme à l'application de la sonde dans la moitié temporale du bulbe (Fig 13) Après l'enucléation nous avons constaté un melanoblastome remplissant le quadrant supérotemporal d'une grandeur de 16 x 10 mm (Fig 14)



FIG 12 Echogramme numero 1492 La malade M D numéro d'observation 1042/62 Diagnostic Melanoblastoma choroideae oc dx La sonde a été appliquée dans le méridien de III h au dessus du limbe contre la tumeur

FIG 13 La meme malade Echogramme numero 1498 La sonde a été appliquée dans le méridien de  $\text{VI } 1/2 \text{ h}$  au dessus de la tumeur

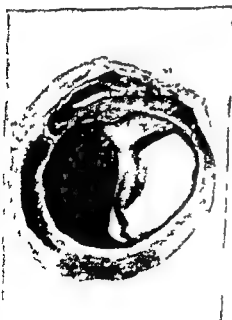


FIG 14 La meme malade Coupe longitudinale du bulbe enucleé montrant la tumeur dans le quadrant supéro-temporal d'une grandeur de  $16 \times 10 \text{ mm}$

9 FN, 58 ans numero 1016/62

Dans l'anamnèse perception visuelle amoindrie de l'oeil droit  
durant quatorze jours

VOD 2 metres et demi doigts

VOS 6/8 + 0,75 D 6/6

Sur le fond de l'oeil il y avait un décollement sphérique de la  
retine s'étendant jusqu'à la papille de IV à VIII h, sans déchirure.  
L'examen avec la lampe de Lange a montré le même rayonnement  
amoindri entre la VI et la VII. La tension intra-oculaire était de  
15 mm/Hg.

L'examen ultrasonique n'a pas réussi à démontrer des échos  
qui auraient fait suspecter une malformation massive, mais seulement  
des échos pathologiques d'une retine décollée. Après un certain temps  
d'observation nous avons pourtant enucleé le bulbe étant suspect  
d'une malformation tumorale. Après l'enucleation nous n'avons pas  
vu de marques d'une tumeur du bulbe droit. Dans le sang nous avons  
constaté par électrophorèse sur le papier une gammaparaprotéinémie.

10 BM 74 ans numéro 1330/62

Dans l'anamnèse perception visuelle limitée de l'oeil droit pendant  
4 mois

VOD 1/2 m doigts etc

VOS 6/15 + 16/10

La retine de l'oeil droit décollée de IV à VIII h jusqu'à la  
papille. La surface de la retine grisâtre brunâtre avec des hémorragies  
isolées. La tension intra-oculaire était de 15 mm/Hg. L'examen avec  
la lampe de Lange a montré un assombrissement total de la pupille  
de V à VIII h. L'examen ultrasonique a démontré des échos patho-  
logiques d'une malformation massive au commencement de  
l'échogramme à l'application de la sonde dans le quadrant inféro-  
temporal. À l'application de la sonde dans le quadrant supéro-nasal  
il y avait de nombreux échos placés à la fin de l'échogramme et  
fondus à l'écho final du bulbe. Par l'examen histologique nous avons  
constaté qu'il s'agissait d'un mélanoblastome de la choroïde d'une  
grandeur de 14 × 5 mm dans le quadrant inféro-temporal.

Par contraste à ce groupe de malades que nous avons du point  
de vue clinique considérés comme suspects d'une croissance de tumeur  
intra-oculaire il y a un groupe de malades où tous les examens  
cliniques ont témoigné pour un simple décollement rétinien.

11 JO 61 ans num 471,62 Dans l'anamnèse il a eu une  
perception visuelle amoindrie de l'oeil droit pendant 1 jour

VOD 2 m kor nel

VOS 2 m — 20 OD 6,36



À l'œil droit décollement sphérique de la rétine dans la moitié supérieure avec une déchirure en fer à cheval dans la périphérie

À 12 h la lampe de Lange brille partout La tension intra oculaire normale L'examen ultrasonique a montré un écho hautement pathologique de la rétine décollée au cours de l'application de la sonde dans la direction opposée du décollement

2 F M, 65 ans, num 1178/62 Dans l'anamnèse elle avait l'impression d'une mouche qui se posait devant l'œil droit, durant 4 mois, et au cours du dernier mois elle se plaignait d'une perception visuelle amoindrie

VOD mouvement, projection correcte

VOS 5/5

La rétine de l'œil droit est décollée dans toute l'étendue de la moitié temporale jusqu'à la papille La lampe de Lange brille partout La tension intra oculaire 15 mm Hg Sans constatation de déchirure L'examen ultrasonique a montré un écho hautement pathologique, revenant complètement à la base temporelle au cours de l'application de la sonde contre le décollement

3 M G, 65 ans, num 1268/62 Dans l'anamnèse épistaxis récurrente, thrombose de la veine centrale de l'œil gauche deux ans auparavant et une vision diminuant rapidement 4 mois auparavant

VOD 5/7,5

VOS : amaurosis

À l'œil gauche dans le corps vitré un nombre de petites opacités La rétine est décollée dans toute son étendue La tension intra oculaire est 12 mm/Hg La lampe de Lange brille dans tous les sens L'examen ultrasonique a montré à l'application de la sonde presque dans tous les méridiens un écho hautement pathologique, dans l'endroit correspondant au sommet de la rétine décollée

4 M V 52 ans, num 1301/62 Dans l'anamnèse il a observé pendant 3 mois qu'il ne voyait pas, en lisant, la partie supérieure des lettres

VOD 5/15 + 1,00 5/15

VOS 5/50 + 2,00 + 2,00 c/t à 90° 5/24

À l'œil gauche la rétine est décollée depuis 3 à 11 h jusqu'à la papille latéralement

L'examen ultrasonique a montré l'écho bas isolé pathologique dans l'endroit du sommet seulement d'un décollement plan de la rétine

5 J A 67 ans num 1292/62 Dans l'anamnèse il a observé pendant 6 semaines une ombre devant l'oeil droit. Après un traitement conservatif dans un autre hôpital il a été envoyé chez nous.

VOD 1 m

VOS 5/5 sl

À l'oeil droit la rétine est décollée dans toute l'étendue de la moitié temporale. L'examen ultrasonique a montré à l'application de la sonde contre le décollement de la rétine 1 haut echo pathologique dans l'endroit correspondant.

Le dix-neuvième jour après une opération réussie du décollement nous avons de nouveau effectué un examen ultrasonique qui a montré un échogramme tout à fait normal sans echo pathologique.

6 F Z 57 ans num 602/62

Dans l'anamnèse une grave myopie bilatérale depuis la jeunesse et une semaine auparavant vision de fils et de taches noires devant l'oeil gauche.

VOD 3/4 m doigts

VOS 2 m éventrement

À l'oeil gauche la rétine est décollée dans toute l'étendue de la moitié temporale jusqu'à la papille. 2 déchirures dans le méridien 1 et 2 h. L'examen ultrasonique a montré à l'application de la sonde à 5 mm du limbe à 7 h un echo pathologique.

7 F H 51 ans num 479/62

Dans l'anamnèse le malade avait été blessé il y a 2 ans 2 fois par contusion à l'oeil droit. Depuis ce temps la perception visuelle de l'oeil droit diminuant graduellement.

VOD mouvement projection du côté nasal defective

VOS 6/6

À l'oeil droit il y a dans le corps vitré de nombreuses hémorragies. La rétine est décollée dans toute son étendue. L'examen ultrasonique a montré un echo pathologique de hauteur moyenne à l'application de la sonde contre la rétine décollée.

III J S 54 ans num 121/62

Dans l'anamnèse après l'extraction d'un corps étranger et l'expulsion des masses cristallines de la lentille il y a eu cinq mois après l'accident un décollement.

VOD 6/6

VOS mouvement projection correcte

Sur le fond de l'oeil droit autant qu'il est possible de la voir à cause d'une cataracte secondaire la rétine est décollée dans toute son

etendue L'examen ultrasonique a montre un echo pathologique d une hauteur moyenne dans l'endroit du decollement en employant une sonde de 10MH<sub>2</sub> = impulsion 1

9 J P 23 ans, num 285/62 Dans l'anamnese le jour de sa venue par hazard constatation d'une maladie de l'oeil gauche

VOD 6/6

VOS 1 metre et quart doigts

La retine de l'oeil gauche est decollée dans toute l'etendue de la moitie temporale et dans le quadrant nasal inferieur Le decollement de la retine de l'oeil serrata entre 4 et 5 h L'examen ultrasonique a montre un echo de hauteur moyenne dans l'endroit du sommet de la retine decollée

10 V B , 37 ans, num 1898/62

Dans l'anamnese une grave myopie bilaterale depuis la jeunesse et pendant les trois derniers jours une perception visuelle diminuee de l'oeil droit

VOD sensibilite a la lumiere projection correcte

VOS 2,5 m doigts — 16 D 6/36

La retine de l'oeil droit est decollée dans presque toute son etendue, il ne reste qu'une mince bande nasale ou elle est adherente L'examen ultrasonique a montre a l'application de la sonde contre de la retine decollée des echos pathologiques sporadiques dans toutes les directions

Si nous apprécions ces deux groupes a leur juste valeur nous pouvons dire que la croissance de tumeurs, soit visible, ou cachee, a toujours au cours de l'examen ultrasonique donne un échogramme caracteristique, compose d'un nombre d'echos pathologiques, entre la retine decollée au dessus de la tumeur et la fin du bulbe pratiquement determine par la paroi sclerotique

Ces echos pathologiques rappellent par leur arrangement les oscillogrammes obtenus dans la defectoscopie technique pour mesurer par exemple la grosseur de la tôle et ils sont proprement dit une suite d'impulsions multiples

Au contraire, ces echos nombreux n'ont jamais etc constatés en cas d'un simple decollement de la retine Nous supposons que le tissu massif de la tumeur a par sa composition donne les conditions necessaires a de nombreux echos d ondes ultrasoniques, tandis que le decollement simple donnait la possibilite d'un echo par la retine decollée et seulement apres, par le tissu du reste adherent de la retine de la choroïde et de la sclerotique Nous avons pris pour tumeur dans le premier groupe aussi un cas d'un simple decollement de la retine chez ce malade nous avons constate en meme temps une parvoproteinémie, et, par mesiance de l'échogramme qui temoignait pour un simple decollement, nous avons effectue l'enucleation du bulbe

(malade décrit dans le premier groupe sous le numero 9) Nous voudrions attirer l'attention sur une constatation typique la tumeur décrite dans le premier groupe comme numero 2 ou une serie d'echos pathologiques apparaissant l'un apres l'autre a ete constatée soit au commencement de l'échogramme ou à la fin de l'échogramme selon que la sonde a été placée contre la sclerotique au dessus de la tumeur ou dans la situation opposée. A cause de la conformité des enregistrements photographiques de ces malades à un simple décollement nous en citons seulement deux cas typiques qui ne diffèrent toutefois guere des autres. Enregistrement au cas décrit sous le numero 3 (Fig 15)



FIG. 15 Echogramme numero 1596 Le malade J. K. numéro d'observation 1292/62 Diagnostic Amotio retinae idiopathica et de La sonde a été appliquée dans le meridian de III h près du limbe

Par les résultats obtenus des deux groupes je suppose qu'il est possible de distinguer avec sûreté par la defectoscopie ultrasonique le décollement secondaire qui recèle une tumeur du décollement primaire de la rétine si la condition est remplie que la tumeur se trouve dans l'axe des rayons émis par la sonde. Théoriquement il serait possible de prendre d'après l'échogramme pathologique une tumeur pour un néoplasme avec décollement qui recèle une exsudation organisée (pseudotumeur).

Dans les derniers temps nous avons tâché d'employer la defectoscopie ultrasonique pour la mensuration de la longueur de l'oeil.

Avec cette méthode il est possible de mesurer la distance entre l'endroit de l'atouchement de la sonde d'oeil c'est-à-dire entre l'épithélium de la corne et le premier tissu dans la partie postérieure de l'oeil donnant un echo, c'est-à-dire la rétine. Du point de vue technique on peut bien lire sur l'échogramme l'echo de l'entrée et le premier d'un nombre d'echos de la paroi postérieure du bulbe qui correspond à la rétine. Pour effectuer cette mensuration il faut que la

distance de deux marques dans la ligne basale de l'image soit 20 mm dans l'eau. Nos mensurations répétées avec nos emetropes sous ses conditions ont déterminé la longueur de la distance entre la corne et la rétine à 1,8 cm.

Toutefois ce résultat était en contradiction avec les mensurations du bulbe pratiquées jusqu'à présent. *Tribulic biologicae* citent que l'axe sagittal de l'œil est d'une longueur de 24 mm. Si nous soustrayons de cette longueur de l'œil, l'épaisseur de la sclérotique 1,3 mm, l'épaisseur de la choroïde 0,3 mm et l'épaisseur de la rétine 0,3 mm, cela fait en tout 1,9 mm. Nous devrions donc obtenir une longueur de 24 mm — 0,9 mm, c'est à dire une longueur moyenne de 22,1 mm, qui représente la distance entre l'épithélium de la corne et la surface de la rétine. Notre résultat qui diffère à peu près de 1 mm est explicable par la vitesse d'une grandeur inégale de la propagation des ondes ultrasoniques dans la corne, dans l'humeur aqueuse, dans le cristallin et dans le corps vitre, qui diffère de la vitesse de la propagation dans l'eau. D'après la vitesse de la propagation des ondes ultrasoniques donnée par le milieu, les ondes ultrasoniques pénètrent par la corne dans 0,516  $\mu$ sec (= 0,8 mm/1,550 mm  $\mu$ sec).

Les ondes ultrasoniques pénètrent par la lentille avec 2,422  $\mu$ sec (= 4 mm/1,650 mm  $\mu$ sec) et par l'humeur aqueuse de la chambre antérieure et par le corps vitre avec 11,47  $\mu$ sec (= 17,2 mm/1,495  $\mu$ sec). Le total des temps ainsi calculés fut 14,408  $\mu$ sec pour la distance de l'épithélium de la corne jusqu'à la rétine, ce qui correspond à une distance véritable de 21,55 mm.

Dans ces citations sur la grandeur inégale de la vitesse de propagation des ondes ultrasoniques par les différents tissus de l'œil, nous expliquons la cause de la différence de la mensuration effectuée avec un appareil calibre pour une vitesse toujours égale de la propagation de l'ultrason dans l'eau. Dans la pratique clinique de la mensuration nous pouvons déduire de ces conclusions mathématiques la nécessité de corriger tous les résultats obtenus jusqu'à présent d'environ 1 mm avec une erreur admissible, que nous n'osons pas déterminer sans examens statistiques étendus, mais que dans cette étape, nous croyons être peu importante.

Après ces mensurations nous avons essayé de mesurer des bulbes ametropiques pour acquérir les expériences nécessaires pour savoir si cette méthode peut servir à un usage pratique. Nos résultats provisoires proviennent d'un nombre relativement petit de bulbes mesurés, même si les différentes mensurations ont été répétées plusieurs fois pour les contrôler.

Nous présentons la revue de ces mensurations dans le tableau numéro 1.

La différence des résultats montre, dans cette étape du travail, que la defectoscopie ultrasonique est capable de résoudre, après élaboration ultérieure, la mensuration de la longueur optique de l'œil in situ. Il faut que le problème de la mensuration du bulbe soit

TABLEAU I — Mesuration de la longueur de l'œil par l'ultrason

Numéro	œil	degré d'amétropie	deduction d'après l'échogramme	longueur corrigée de 4 mm
1	gauche	— 14	2 3 cm	2 7 cm
2	droit	— 8	2 13 cm	2 53 cm
3	droit	— 13	2 28 cm	2 68 cm
4	gauche	— 7	2 12 cm	2 52 cm
5	droit	— 20	2 62 cm	3 02 cm
6	gauche	— 17	2 46 cm	2 82 cm
7	droit	— 16	2 56 cm	2 96 cm
8	gauche	— 7	2 12 cm	2 52 cm
9	droit	— 16	2 44 cm	2 94 cm
10	gauche	— 14	2 27 cm	2 67 cm

elabore et que les résultats acquis avec la déféctoscopie ultrasonique soient vérifiés par d'autres méthodes. C'est là que je vois la tâche ultérieure de ce travail.

**Conclusion.** Les auteurs décrivent leurs expériences dans la différenciation entre le simple décollement de la rétine et le décollement recelant une tumeur. Ils supposent que d'après les résultats actuels les nombreux échos pathologiques typiques sont un signe sûr de la croissance d'une tumeur solide intra-oculaire de même que l'écho pathologique isolé est la marque d'un décollement simple, sous lequel se trouve seulement le liquide homogène sous-rétinal. Les résultats actuels montrent que par la déféctoscopie ultrasonique on peut mesurer avec précision la longueur de l'axe optique de l'œil in situ.

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Numéro	œil	degré d'anisotropie	deduction d'après l'échogramme	longueur corrigée de 4 mm
1	gauche	— 14	23 cm	27 cm
2	droit	— 8	213 cm	253 cm
3	droit	— 13	228 cm	268 cm
4	gauche	— 7	212 cm	252 cm
5	droit	— 20	267 cm	302 cm
6	gauche	— 17	246 cm	282 cm
7	droit	— 16	256 cm	296 cm
8	gauche	— 7	212 cm	252 cm
9	droit	— 16	244 cm	294 cm
10	gauche	— 14	227 cm	267 cm

elaboré et que les résultats acquis avec la defectoscopie ultrasonique soient vérifiés par d'autres méthodes. C'est là que je vois la tâche ultérieure de ce travail.

**Conclusion.** Les auteurs décrivent leurs expériences dans la différenciation entre le simple décollement de la rétine et le décollement recelant une tumeur. Ils supposent que d'après les résultats actuels les nombreux échos pathologiques typiques sont un signe sûr de la croissance d'une tumeur solide intra-oculaire, de même que l'écho pathologique isolé est la marque d'un décollement simple, sous lequel se trouve seulement le liquide homogène sous-rétinal. Les résultats actuels montrent que par la defectoscopie ultrasonique on peut mesurer avec précision la longueur de l'axe optique de l'œil in situ.

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## THE PURPOSE OF CALIBRATION BY DYNAMOMETRY

E. WEIGELIN (BONN GERMANY), A. IOBSTEIN  
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(Bern Switzerland)

Ophthalmodynamometry is today a valuable method for clinical investigations. The results are very clear when the investigation is performed on cases with stenosis and a blockage of one carotid artery, as then the extremely diminished values of the affected side can be discovered. Usually it is sufficient to find out whether the pulsating collapse of the central artery on the papilla takes place when the eye is subject to stress in varying degrees from the dynamometer. A difference of 20% is usually significant.

This is a simple test by which a blocked carotid can be diagnosed from the positive result, if the anatomical structure of both eyes is similar and if the central retinal artery is not blocked. The negative or doubtful result of the test is insignificant. In about a half of our cases with blockage of the carotid or stenosis the readings were about the same in both eyes.

When that degree of stress is reached which upsets the circulation in the central artery then there is a more significant difference between the two readings. For this a stronger dynamometric pressure must be applied which some authorities consider dangerous. From more than forty thousand investigations in Strasbourg and Bonn we have found only a very few who suffered temporary disturbances. With this test, all except about 15% of cases of unilateral carotid thrombosis can be diagnosed. This shows also that the negative result very probably proves the absence of this disease.

Difficulties in diagnosing a carotid thrombosis with the ophthalmodynamometer arise when (Fig 1)

- (1) the disease is bilateral
- (2) glaucoma is present with varying tension
- (3) a high grade anisometropia is present
- (4) a central artery blockage is present either on the affected or on the other side
- (5) dynamometric investigation on the non affected side is impossible owing to anophthalmus, cataract etc.

Some of these conditions are very seldom present others particularly the bilateral carotid stenosis have often been observed in the

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## THE PURPOSE OF CALIBRATION BY DYNAMOMETRY

E. WEIGELIN (BONN GERMANY), A. IOBSTLEIN  
(STRASBOURG FRANCE), and P. NIESEL  
(Bern, Switzerland)

Ophthalmodynamometry is today a valuable method for clinical investigations. The results are very clear when the investigation is performed on cases with stenosis and a blockage of *one* carotid artery, as then the extremely diminished values of the affected side can be discovered. Usually it is sufficient to find out whether the pulsating collapse of the central artery on the papilla takes place when the eye is subject to stress in varying degrees from the dynamometer. A difference of 20% is usually significant.

This is a simple test by which a blocked carotid can be diagnosed from the positive result if the anatomical structure of both eyes is similar and if the central retinal artery is not blocked. The negative or doubtful result of the test is insignificant. In about a half of our cases with blockage of the carotid or stenosis the readings were about the same in both eyes.

When that degree of stress is reached which upsets the circulation in the central artery then there is a more significant difference between the two readings. For this a stronger dynamometric pressure must be applied which some authorities consider dangerous. From more than forty thousand investigations in Strasbourg and Bonn we have found only a very few who suffered temporary disturbances. With this test all except about 15% of cases of unilateral carotid thrombosis can be diagnosed. This shows also that the negative result very probably proves the absence of this disease.

Difficulties in diagnosing a carotid thrombosis with the ophthalmodynamometer arise when (Fig 1)

- (1) the disease is bilateral
- (2) glaucoma is present with varying tension
- (3) a high grade anisometropia is present
- (4) central artery blockage is present either on the affected or on the other side
- (5) dynamometric investigation on the non affected side is impossible owing to anophthalmus, cataract etc.

Some of these conditions are very seldom present, others partly. The bilateral carotid stenosis have often been observed in the

last years, some conditions are easy to recognise, for instance anisometropia, others like glaucoma and bilateral carotid stenosis prevent us from making our investigations successful. Because the test is not sufficient in these cases, we must take an additional measurement

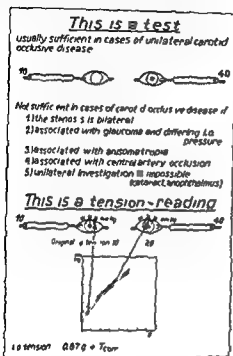


FIG 1

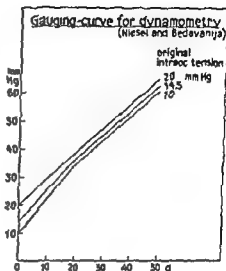


FIG 2

If we take into consideration the original tension in the eye, we can find out the diastolic and systolic blood pressure in the ophthalmic artery with dynamometry. Scidel, Duke Elder and Friedenwald discovered this long time ago. To measure the blood pressure, a unit must be used with which pressure in a fluid system can be measured. In Biology this unit is usually mm Hg.

To find out how high the tension is, when the eye is subject to a particular stress (in g), it must be measured with the applantation tonometer (DRAEGLR), while the eye is subject to that amount of stress. More simple still, a graph can be plotted. We have done this in Bonn and Strasbourg with modern manometric methods on living, and dead eyes and using the applantation tonometer. The results from different methods are the same: the values obtained are about the same as those which we could expect from our knowledge of the physiology of the blood circulation. These values are also proved by manometric parallel measurements in the internal carotid artery. Here is the graph used by us (Fig 2) and which was originally produced by Niesel and Bedavanya from applantation tonometry. Today we can measure a true blood pressure of the ophthalmic artery by using the eye as a manometer.

Of course it is easier to measure the blood pressure on the upper arm. But then it can only be estimated whether the pressure is high,

low or normal. If we measure the blood pressure in two different places we can produce more exact information. We must first know the relative values of the two pressures. They are very close. The correlative coefficient amounts to about 0.9 for the diastolic values (Fig 3). BJÖRK found the same. If one uses the middle pressure obtained from the diastolic and systolic value in both places of measurement like WEZLER and BÖGER, then the correlation becomes still higher. It now amounts to 0.94 or 0.955 if the original tension in the eye is taken into consideration. This means that these values are 91% dependent on each other. Even if our gauging today is not always so accurate a method for investigation can easily be constructed from this basis if

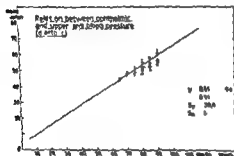


FIG 3

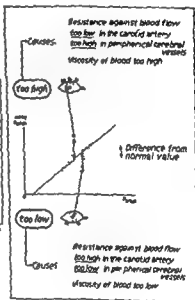


FIG 4

- (1) there are pathological cases which are scattered outside the normal variations
- (2) the causes leading up to pathological values are known

(Fig 4) In our book which has also now been published in English, the physical fundamentals of the method have been described in detail. I would like to say here quite shortly that the pressure in the ophthalmic artery is too low in relation to the upper arm pressure when

- (1) there is a raised resistance in the carotid artery usually on account of stenosis and occlusion. When these are unilateral then as previously mentioned the values of the two sides are different



- (2) there is a decrease of the peripheral resistance in the brain vessels. This is often present with vasomotor headaches.

Conversely the pressure in the ophthalmic is relatively higher than that in the upper arm when

- (1) resistance in the carotid artery is decreased on account of dilatation
- (2) resistance in the peripheral intracranial vessels is increased. This is found in cases with the constricted type of vasomotor headaches and with most types of hypertension. From the relative values of the two pressure measurements and a further formula which makes possible the differentiation between distal and proximal circulatory disorders, we can diagnose bilateral carotid thrombosis, carotid stenosis in a monocular patient when the remaining eye is on the affected side, and the already quoted combinations. In addition, it is possible to recognise peripheral intracranial circulatory disorders. The application of dynamometry has therefore very wide possibilities.

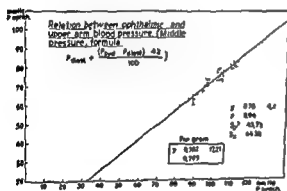


FIG 5

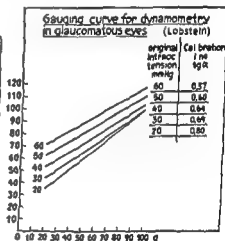


FIG 6

You will want to know whether the same results can be achieved without converting the g values which can be read directly from the dynamometer into the mm Hg values. The answer is no. The correlation between the g values of the dynamometer and the upper arm pressure, without considering the tension in the eye, is less exact and much lower ( $P < 0.01$ ) than the relative ophthalmic pressure. The mutual influence amounts to only 61% in this case against 91%. The separation of the normal from the pathological cases is therefore much more difficult (Fig 5). This is because the graph is not linear — (Fig 1). It is only linear during its middle course. At the beginning it rises steeply and in its higher region, which has not yet been accurately plotted, it is flatter. Raised tension in the eye before it is subjected to the stress from the dynamometer, greatly influences the gradient of the graph (Fig 6). This is very important if dynamometry is used for

glaucoma research. When the eye is subject to a 30 g stress taken from differing tensions the results differ considerably for the ophthalmic pressure if for instance the diastolic criterion is released.

This simple dynamometric test is very useful in recognizing unilateral stenosis and occlusion of the carotid. When performed as a more complex examination to measure the blood pressure dynamometry could become still more useful for research in circulatory disorders and probably also in glaucoma. As the subject has been dealt with on a mathematical basis it is much easier to carry out the investigation and to estimate the results as all necessary data is at our disposal on a few charts.

Unfortunately it is not possible to describe here the stages of the investigation in detail.

- (2) there is a decrease of the peripheral resistance in the brain vessels. This is often present with vasomotor headaches.

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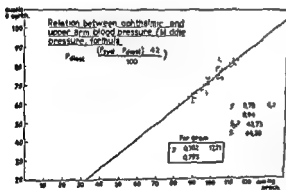


FIG 5

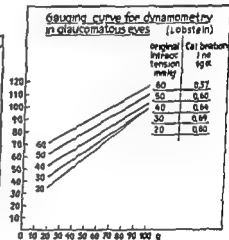


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TABLE 1 — *Tumours of the Orbit*

(A) Primary tumours	(B) Secondary tumours	(C) Metastatic tumours	(D) Orbital tions of disease	Manifesta tions of generalised disease
(i) Mixed tumours of the lacr gland 16	(a) Globe	(a) Ad Gland or para gln	(i) Lymphatic leucaemia	3
(ii) Dermoid cyst 15	Retino-blastoma III	Sympathicoblastoma	(ii) Chloroma	2
(iii) Haemangioma 14	(b) Lids —	(b) Lung —	(iii) Hand Schuller Christian disease	1
(iv) Lymphoma 14	Epithelioma 2	Carcinoma	Total	6
(v) Lymphosarcoma 10	(c) Antrum —	Total		
(vi) Schwannoma 8	Sq cell carcinoma 1			
(vii) Undifferentiated Sarcoma 6	Total 41			
(viii) Leucemia 6				
(ix) Glioma 5				
(x) Neurofibroma 5				
(xi) Lipoma 5				
(xii) Meningioma 3				
(xiii) Rhabdomyosarcoma 3				
(xiv) Fibroma 2				
(xv) Angiosarcoma 2				
Total 114				

## TUMOURS OF THE EYE\*

S P DAS,

Institute of Ophthalmology, Medical College Hospitals,  
Calcutta (India)

600 cases of tumours of the eye were examined histopathologically in the pathology department of the Institute of Ophthalmology, Calcutta over a period of 12 years (1950-1961). All these tumours were divided into 5 groups according to their sites

- I Tumours of the Orbit
- II Intraocular tumours
- III Tumours of the lids
- IV Epibulbar tumours
- V Tumours of the lacrimal passages

### I Tumours of the Orbit —

The common tumours of the orbit from the present series of 160 cases are indicated in table 1 on page 1375

- 1 Secondary retinoblastoma
- 2 Mixed tumours of the lacrimal gland
- 3 Dermoid cyst
- 4 Haemangioma
- 5 Lymphoma
- 6 Lymphosarcoma

Retinoblastoma will be dealt with the connection of intraocular tumours

### MIXED TUMOURS OF THE LACRIMAL GLAND

In the present series of sixteen cases of mixed tumours of the lacrimal gland, ten were histologically benign and six were malignant. Three benign tumours later on turned into malignant and two of them died, and the other one is symptom free now. So histological diagnosis of the benignity of mixed tumours of the lacrimal gland is no sure guide to the prognosis of the patient. Four malignant cases died due to intracranial extension and the rest are symptom free now after radical surgery and postoperative deep X ray therapy

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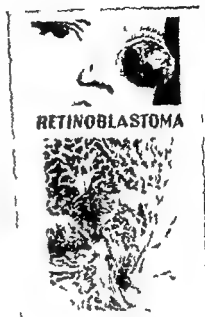
\* Read at the XX International Congress of Ophthalmology held in New Delhi 1962

**HAEMANGIOMA**

Twelve of the fourteen cases of haemangioma of the orbit were of cavernous variety. Surgical removal and irradiation were the two methods of treatment adopted. Observing the complications of irradiation in two cases surgical removal was employed in twelve cases and the results are satisfactory.



V Lymphosarcoma of the Orbit



VI Retinoblastoma

**LYMPHOMA**

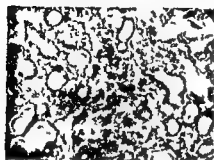
Lymphoma may be benign or malignant and it may be associated with leucaemic blood picture. Nine cases could be followed up from the series of fourteen. Two cases later on showed typical leucaemic blood picture and died. Two other cases showed malignant character in later biopsies. So in benign lymphoma repeated biopsies and blood count are necessary. Five patients are doing well at present after irradiation therapy.

**LYMPHOSARCOMA**

Seven of the present series of ten lymphosarcoma showed localised lesions in the orbit. Three patients with generalised metastasis died within a year. Three other patients are doing well for nearly three years after surgery and radio therapy. Two patients refused operation but were given irradiation therapy and are known to have died after multiple manifestations. No follow up data was available in other two cases.



**MIXED TUMOUR OF THE  
LACRIMAL GLAND**



**I Mixed Tumour of the lacrimal  
gland**



**DERMOID CYST  
OF THE ORBIT**



**II Dermoid Cyst of the Orbit**

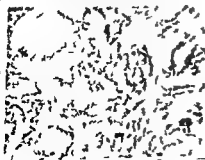
#### **DERMOID CYST**

All the present fifteen cases of dermoid cysts of the orbit were noted in the second and third decades of life

The usual treatment of complete operative removal was adopted in all cases and there was no recurrence



**HAEMANGIOMA  
OF THE ORBIT**



**III Haemangioma of the Orbit**



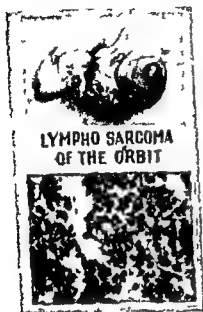
**LYMPHOMA OF  
THE ORBIT**



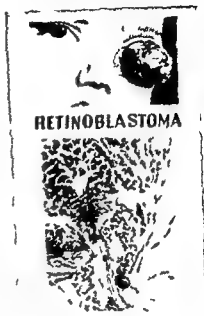
**IV Lymphoma of the Orbit**

**HAEMANGIOMA**

Twelve of the fourteen cases of haemangioma of the orbit were of cavernous variety. Surgical removal and irradiation were the two methods of treatment adopted. Observing the complications of irradiation in two cases surgical removal was employed in twelve cases and the results are satisfactory.



V Lymphosarcoma of the Orbit



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## II Intraocular Tumours

160 cases of intraocular tumours were examined histopathologically (Table No II) Of these 148 cases were retinoblastoma

TABLE II — *Intraocular Tumours*

Lists

1	Retinoblastoma	148
2	Malignant melanoma of Choroid	5
3	Haemangioma of Choroid	3
4	Leucaemia	2
5	Malignant Melanoma of Ciliary Body	1
6	Metastatic Carcinoma of Choroid from breast	1
Total		160

### RETINOBLASTOMA

The average age of the present series of cases was 3.8 years. The oldest one was 20 years and the youngest one was one month old. The disease was bilateral in 29% of cases. All cases were sporadic except one where patient's mother was a retinoblastoma survivor. Three instances of familial incidence were noted in this series and in



EPITHELIOMA  
OF THE LID



VII Epithelioma of the Lid



PAPILLOMA  
OF THE LID



VIII Papilloma of the Lid

one family none of the five children survived from retinoblastoma, although the parents were free from the disease. Histologically, rosette formation was noted in 68% cases and optic nerve extension was observed in 44% cases. The tumour possesses a poor prognosis. 37 bilateral cases could be followed up and none of them is known to have survived. Only 14 cases are known to be living at present from the 86 unilateral follow of cases. Spontaneous regression was noted in two cases where the eyes resulted in phthisis bulbi.

### III Tumours of the Lids

Out of 170 cases of tumours of the lid, the common tumours are (Table III) —

TABLE III — Tumours of the lids

1 Epithelioma	52
2 Haemangioma	32
3 Papilloma	17
4 Fibroma	15
5 Dermoid	14
6 Naevus (Melanotic)	10
7 Lipoma	7
8 Sarcoma	6
9 Adenoma of sebaceous gland	3
10 Adenocarcinoma of Meibomian gland	3
11 Malignant Melanoma	3
12 Lymphoma	2
13 Lymphosarcoma	2
14 Neuroma	2
15 Adenoma of Meibomian gland	1
16 Adenocarcinoma of sweat gland	1
Total	170

- 1 Epithelioma
- 2 Haemangioma
- 3 Papilloma
- 4 Dermoid
- 5 Fibroma

#### EPITHELIOMA

Of the 52 cases of epithelioma of lids 46 were basal cell variety and the rest were squamous cell variety. Only two cases came in the late stage where there was invasion of the lids, conjunctiva and the orbit. One of them is known to have died and the other symptom free now. The usual treatment adopted in all cases was complete and wide excision followed by irradiation. Special care was taken in determining the extent of the lesion and the excision was done beyond the site of the

lesion. In the majority of the cases lower lids were affected and this was helpful in the plastic repair.

#### PAPILLOMA

Papillomas are benign, but rarely may undergo malignant change. One of the present 17 cases was malignant (early stage). Good result was obtained by simple excision of the tumour. Another one of these cases showed recurrence, but this was not followed by malignant change.

#### FIBROMA

Excision was the treatment. No recurrence or the malignant change was observed in the present 15 cases.

Haemangioma and the dermoid have already been discussed in connection with the orbital tumours.

### IV Epibulbar Tumours

The common epibulbar tumours from the present observation of 154 cases are as follows (Table No IV)

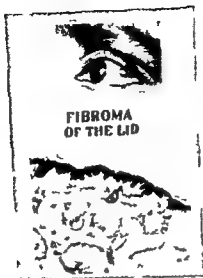
TABLE IV — Epibulbar Tumours

Lists

(i) Dermoid	28
(ii) Epithelioma	27
(iii) Haemangioma	23
(iv) Fibroma	22
(v) Papilloma	16
(vi) Naevus	15
(vii) Lipoma	9
(viii) Lymphoma	5
(ix) Adenoma	4
(x) Malignant Melanoma	3
(xi) Sarcoma	1
(xii) Teratoma	1
Total	154

- 1 Dermoid
- 2 Epithelioma
- 3 Haemangioma
- 4 Fibroma
- 5 Papilloma

All these tumours have already been discussed in connection with the tumours of the orbit and the tumours of the lids.



IX. Fibroma of the Lid

#### V Tumours of the Lacrimal Passages

The only tumour noted in this connection was a carcinoma of the lacrimal sac

#### COMMENT

Tumours of the eye is a vast subject but when the tumours of the different sites are considered together, many tumours are found to be common and the subject then appears easier

Although the list of orbital tumours is large the common tumours form the majority of the cases. From the clinical point of view the subject can be made simpler if the tumour is called by its basic name and not by the various descriptive terms. For example for mixed tumour of the lacrimal gland there are such names as adenocarcinoma, cylindroma, adenoid cystic epithelioma, myxo-chondrocarcinoma and adenoma. The treatment of the different orbital tumours depends on the correct diagnosis. For instance for mixed tumour of the lacrimal gland treatment is radical surgery followed by post operative deep X ray therapy for lymphoma and lymphosarcoma deep X ray therapy for haemangioma, surgery or deep X ray therapy.

Retinoblastoma is not only the commonest intraocular tumour but also the most common tumour of the eye in the present observation. Only 14 cases from the present series of 148 retinoblastoma are living at present. The poor result of the present observation was due to delay in coming in the early stage of the disease, high incidence of bilaterality, early metastasis particularly tumour extension via the optic nerve even before the appearance of proptosis.

Epitheliomas of the lids and epibulbar regions possess a good prognosis. Only one case from the present series of 79 epitheliomas is known to have died. This satisfactory result of the present observation was due to early diagnosis, complete and wide excision of the tumour and the post operative deep X-ray therapy.

### SUMMARY

650 cases of tumours of the eye were examined histopathologically in the pathology department of the Institute of Ophthalmology, Calcutta (INDIA) over a period of 12 years. The common tumours have been briefly discussed.

### ACKNOWLEDGEMENT

I am indebted to Prof K. L. Sen, Director, Institute of Ophthalmology, Calcutta for the encouragement in writing this paper and the kind permission for publishing the same. I am grateful to Dr P. K. Sarkar, Pathologist and to Mr A. Das Gupta, Artist for all possible help in this paper.

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**LIST OF BOOKS EXHIBITED AT THE XIXth INTERNATIONAL  
CONGRESS OF OPHTHALMOLOGY—DONATED TO THE ALL  
INDIA OPHTHALMOLOGICAL SOCIETY**

<i>Name of the Book</i>	<i>Author</i>	<i>Published by</i>
1 GLAUCOMA	Dr Sidney Lerman	Messrs Charles C. Thomas U S A
2 NIGHT VISION	Dr Jayle Gaetan E	do
3 OPTICS	Dr Kenneth N Ogle	do
4 ATOPIC CATARACT	Dr Emanuel Rosen	do
5 PRINCIPLES OF OPHTHALMOLOGY	Dr John H Erbaugh	do
6 THE AQUEOUS VENS	Dr Karl W Ascher	do
7 EYE SIGNS IN GENERAL DISEASE	Dr F Herbert Hoessler	do
8 GEOGRAPHIC OPHTHALMOLOGY	Dr Holmes	do
9 CLINICAL ELECTRO- RETINOGRAPHY	Dr Jerry Hart Jacobson	do.
10 THE TRANSPARENCY OF THE CORNEA	—	Messrs Blackwell Scientific publica tions Ltd Oxford
11 LECTURE NOTES ON OPHTHALMOLOGY	Dr Patrick D Trevor Roper	do
12 BIOCHEMISTRY OF THE EYE	Dr Antonette Pisci & Dr Rum Van Heyningen	do
13 GLAUCOMA	—	do
14 ENDOGENOUS INFLAMMATIONS OF THE LVEAL TRACT	Dr Alan C Woods	Messrs Baillière Tin dall and Cox Ltd London
15 CLINICAL NEURO- OPHTHALMOLOGY	Dr Frank D Walsh	The Williams and Wilkins Co U S A
16 MEDICAL DICTIONARY	Stedman	do
17 THE STRUCTURE OF THE EYE	Dr George A. Smelser	Messrs Academic Press Inc London
18 THE EYE—1st volume	Dr Hugh Davson	do
19 SYSTEM OF OPHTHALMOLOGY (Vol VII)	Sir Stewart Duke Elder	Henry Hampton London
20 OPHTHALMOLOGIC DIAGNOSIS	F Herbert Hecaller	—
21 OCULAR ALLERGY	Dr Frederick H Theodore & Dr Abraham Schlossmann	—

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**3rd December 1962**

Callahan, A (U S A)	Symposium on entropion surgery for different types
Hughes W L (U S A) and Orkan G Stasior	Techniques of obtaining fascicula for grafting
Hikaru H (Japan)	Automatic recording of visual acuity in vision testing
Fox S A (U S A)	Senile entropion surgical correction
Shigeharu Okamoto (Japan)	A new surgery against obstruction of nasolacrimal duct with or without dacryocystitis
Rais Hadi (Tunisia)	Lamellar keratoplasty in corneal fistula
Barrquer, J (Colombia)	Experimental refractive surgery
Marcel Noix (France)	Etude dynamique direct et radiologique de differents phenomenes oculaires
Gunther, G (W Germany)	Objective determination of visual acuity

**4th December 1962**

Castroviejo R (U S A)	Instrumentations techniques and results in keratectomies
Cooper S N (India)	Circular guide and knife
Hervouet F (France)	Les taturages de la corne
Casonavas J (Spain)	Hering's ring and its modification
Cupra U C (India)	Trichoma

**5th December 1962**

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Schumck R A (U S A)	Use of air in excluditis clefts
Sinskey R M (U S A)	A surgical procedure for the improvement of congenital nystagmus
Agarwal I I (India)	Retinitis pigmentosa - a new therapeutic approach
Chandra D B (India)	Cataract extraction - a modified technique
Suzumura A (Japan)	New measurement apparatus of accommodation (An H S Autograph asthenopia meter)
Eusebio J (Philippines)	Scleral transposition in selected diseases of the optic nerve and retina

Hagino R (Japan)

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A new technique for operation of retinal detachment — the intrascleral pocket

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# **SYMPOSIUM III**

## **EALES S DISEASE**

**SYMPOSIUM IV**

**PROBLEMS RAISED IN OPHTHALMOLOGY BY THE  
RECENT PROGRESS IN AVIATION**



# VISUAL ACUITY AND OCULAR MUSCLE BALANCE REQUIREMENTS IN MODERN AVIATION

By Wing Commander T G JONES

*India*

## INTRODUCTION

Every conscious moment we are constantly fed by our eyes with information as to the nature of objects in our environment and as to their location in space. The first is the function of visual acuity, the second of depth perception. The piloting of high performance aircraft require a high performance of both these functions. I will briefly review the qualities of these functions that are required for in jet age pilots and will discuss whether the present day standards and the ophthalmic examination in routine use to ensure the fulfilment of these standards meet these requirements in the light of experience in the Indian Air Force.

## VISUAL ACUITY

Out of Nicholls's<sup>26 27 28</sup> comprehensive study on the relation ship of heterophoria to depth perception in aviation, the one very definite fact that emerged was the co relation between visual acuity and flying performance. The high altitudes and the high speeds attained by present day aircraft adversely influence the pilot's visual acuity efficiency.

At high altitudes the flyer is frequently faced with an empty visual field. Whiteside's<sup>27 28</sup> investigation on the effect of this empty visual field on visual performance reveal that under these conditions, the emmetropic eye seems to rest on an accommodation level of +0.5 D, this may be boosted upto +1.5 D by the pilot's efforts to search for his target. The resulting myopia doubles the minimum visual angle thereby reducing pick up range to half the normal. Target detection is further hampered by the lack of sufficient contrast between the object and its surroundings. The absence of any back ground to provide parallax displacement renders movement discrimination and judgement very difficult.

The pick up range is determined by the resolving power of the eye. The higher the resolving power the greater the pick up range and the more time the pilot has at his disposal to decide upon and carry out a course of action. This is amply illustrated in Table I on page 889.

It must be appreciated that the images of objects first sighted usually first strike the peripheral retina which has a lower resolving power, requiring twice the foveal threshold size at 5° from the fovea,

and four times the foveal threshold size at  $10^\circ$  from the fovea. The presence of a refractive error will considerably raise these thresholds.

TABLE I *Pick up ranges for a fighter aircraft (fuselage dimension 84') and time intervals at 1800 m p h for various visual acuity levels*

Visual Acuity	Pick up range (miles)	Time interval (in seconds)
6/12	2.2 miles	4.4 secs
6/9	2.9 miles	5.9 secs
6/6	4.4 miles	8.9 secs
6/5	5.3 miles	10.7 secs
6/4	6.6 miles	13.3 secs

The speed of the visual perception is woefully inadequate to meet the demands of modern aircraft, and this combined with the difficulty of seeing at altitudes is a major factor in mid air collisions. Byrnes<sup>45</sup> and Strughold<sup>31</sup> have shown that the small time intervals of the chain of latencies of visual perception assume importance in the background of the speeds attained by present day aircraft. Table II, gives these time intervals and the distances covered during these intervals at speeds of 600 m p h and 1800 m p h.

TABLE II — *Time intervals and distances travelled between first sighting an object and changes of flight paths (after Byrnes)*

Operation	Time in seconds		Progressive distance travelled in feet	
	For operation	Progressive total	at 600 m p h 880 /sec	at 1800 m p h 2640 /sec
I Perception and extra foveal to foveal perception (Minimum recognition)	1.045	1.045	924	2.759
II Decision and motor response	2.40	3.445	3.032	9.095
III Aircraft response	2.0	5.445	4.792	14.375

These time intervals are absolute minima and vary with the intensity and wave length of the stimulus, the region of the retina stimulated and its state of adaptation. Any factor causing a fall in the



visual acuity, such as the refractive error, obstructions to vision, dirty windshields and visors, acceleration forces, anoxia and fatigue will greatly stretch these time intervals.

The total time interval from extra foveal perception to aircraft response is 5.445 sec. Table I shows that with 6/9 vision, the pilot has a pick up range of 2.9 miles giving him 5.9 seconds at a closing speed of 1800 m.p.h., and so just meets these requirements. Hence, it follows that the minimum uncorrected binocular vision for a pilot of present day aircraft should not be below this level. Fast mechanical adjustment of the eyes should be included in the criteria for assignment to high speed aircraft, and the effects of age on the speed of these adjustments should also be taken into account.

Much research effort has been expended to lessen the pilot's visual load and to make good his deficiencies—in many cases however this has merely resulted in the transfer of the visual task from outside to inside the cockpit and has created new problems.

The use of radar requires the pilot or the navigator to observe very attentively at near distance, a fluorescent screen on which are brightening and fading aggregations of relatively dim points of lights on a dark background and to make a rapid and accurate interpretation of the display. Gerathewohl<sup>18</sup> has determined that the eye movements in radar operations are complex and are carried out in jerks. The duration of movement vary with the task from 20 to 25 ms. The duration of fixation ranges from 130 ms for an orientation task to 1815 ms for a bombing task. The straining of the eyes in this unusual manner may result in fatigue, drowsiness, asthenopia and headaches.

According to Bellecci,<sup>2</sup> heterophoria, hypermetropia and mild anisometropia hinder visual performance and predispose to visual breakdown. Riffenburgh<sup>19</sup> recommends that the radar operator should look away to relax his accommodation every third or fourth sweep.

The change of fixation from scope to instrument panel and to outside the cockpit require the eyes to rapidly adapt through a wide variation of brightness levels. According to Herrick and his co-workers<sup>20</sup> aircrew viewing a C.R.T. display experience a fall in visual efficiency impairing the ability to read instruments and to perceive objects external to the aircraft. Efficient visual function under these conditions demand good near visual acuity with speedy accommodation, speedy visual reactions and binocular vision at near distances.

Since the wearing of correcting lenses by pilots of modern high speed aircraft is problematical and not accepted universally, a high degree of uncorrected visual acuity is required to meet these demands. Visual standards in the Indian Air Force have always demanded 6/6 vision in one eye and 6/9 vision in the other, correctable to 6/6, manifest hypermetropia being limited to +2.25 D.

Analysis of 2,266 examinations conducted at the Central Medical Establishment<sup>11</sup> reveal that (79.8%) of candidates accepted under these standards have an unaided binocular vision of at least 6/5, thereby fully meeting the demands of modern flying. Of the serving aircrew, ages ranging from 20 to 45 years reviewed, (84.1%) had unaided binocular vision of 6/5 and only 2.8% had unaided binocular vision lower than 6/12 — the extreme limit being 6/36 — 6/60, with a refraction of  $-1.5$  D.

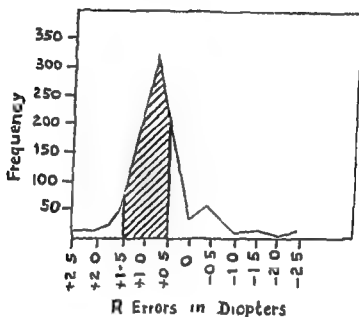


FIG 1

Distribution of refractive errors in accepted candidates and in serving aircrew

The distribution of the refraction in accepted candidates and in serving aircrew is shown in Fig 1. This shows that 80% have a refractive ranging from  $+0.5$  D to  $+1.5$  D. This has two advantages. Firstly, this range of refraction neutralises the myopia of the empty visual field and is ideally suited for search at high altitudes. Secondly, this range of refraction is sufficient to offset the myopic tendencies that occur between the 20 and 30 years, which, Diamond<sup>12</sup> and Howard<sup>13</sup> & Slapater<sup>14</sup> have estimated as an annual shift of  $-0.05$  D.

Analysis of the refraction in relation to their visual acuity is shown in Table III on page 892.

At the 6/6 level, the refraction may range from  $-1.5$  D to  $+3.5$  D. The norm for myopia being  $-0.5$  D and that for hypermetropia  $+0.75$  D. At the 6/9 level, the refraction range was from  $-2.5$  D to  $+4.5$  D. The norm for myopia being  $-0.75$  D and that for hypermetropia  $+1.5$  D. The inaccuracy of visual require

TABLE III — *The limits of refractive errors encountered together with the mean and modal refraction at each visual acuity level*

Visual Acuity	Myopic limit	Hypermetropic limit	- Error		+ Error	
			Mean	Mode	Mean	Mode
6/5	-0.5D	+2.5D	-0.25D	-0.25D	+0.75D	+0.75D
6/6	-1.5D	+3.5D	-0.50D	-0.50D	+0.80D	+0.75D +1.0D
6/9	-2.5D	+4.5D	-1.0D	-0.75D	+1.24D	+1.25D +1.5D

ments in terms of visual acuity alone without considering the refraction becomes evident. Diamond<sup>10</sup> recommends that the requirement for airline pilots should be 6/6 vision with a refraction of not less than +0.5 D to neutralise the myopia shift of the 20-30 year range and not more than +1.0 D to offset any deterioration that might occur due to the pre-presbyopic hypermetropic shift. This will safeguard against the loss of experienced pilots due to acquired visual defects and will ensure a high standard of visual efficiency over a 10 to 15 year period. This however is an ideal requirement; a more practical approach demands further investigation to widen these limits.

#### DEPTH PERCEPTION AND OCULAR MUSCLE BALANCE

No aspect of vision in aviation has been more extensively investigated and has led to more diversity of opinion than depth perception and its relation to ocular muscle balance. Experience in World War I showed that 70 to 80% of accidents were due to bad landings and according to Clements<sup>16</sup> these were mainly caused by heterophoria made manifest by fatigue. Howard<sup>17, 18, 19</sup> in an analysis of World War I accidents concluded that the judgement of distance was mainly dependent on good and equal vision in the two eyes, and that the main factor was binocular parallax. This observation resulted in the Howard-Dolman test which has ever since been used as a criterion for the depth perception ability necessary for flying. Ocular muscle imbalance was viewed with concern and Doyné<sup>11</sup> held that heterophoria often implied the unequal action of the extraocular muscles resulting in a bilateral visual disharmony. He considered a one-eyed man with acquired stereoscopic vision less dangerous for flying than a two-eyed man whose eyes may be unreliable. These views resulted in very stringent standards for heterophoria being laid down at the Peace Convention in 1917 and agreed on for international use by the medical sub-committee of the International Commission for Air Navigation at Rome in 1927. These prevailed up to the beginning of World War II.

Analysis of 2,266 examinations conducted at the Central Medical Establishment<sup>20</sup> reveal that (79.8%) of candidates accepted under these standards have an unaided binocular vision of at least 6/5, thereby fully meeting the demands of modern flying. Of the serving aircrew, ages ranging from 20 to 45 years reviewed, (84.1%) had unaided binocular vision of 6/5 and only 2.8% had unaided binocular vision lower than 6/12 — the extreme limit being 6/36 — 6/60, with a refraction of — 1.5 D.

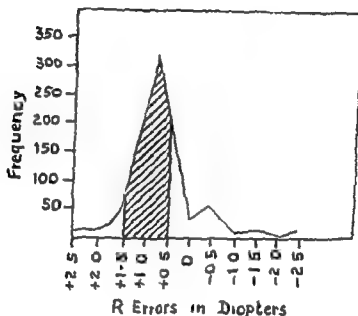


FIG 1

Distribution of refractive errors in accepted candidates and in serving aircrew

The distribution of the refraction in accepted candidates and in serving aircrew is shown in Fig. 1. This shows that 80% have a refraction ranging from +0.5 D to +1.5 D. This has two advantages. Firstly, this range of refraction neutralises the myopia of the empty visual field and is ideally suited for search at high altitudes. Secondly, this range of refraction is sufficient to offset the myopic tendencies that occur between the 20 and 30 years, which, Diamond<sup>9</sup> and Howard<sup>16</sup> & Slapier<sup>22</sup> have estimated as an annual shift of — 0.05 D.

Analysis of the refraction in relation to their visual acuity is shown in Table III on page 892.

At the 6/6 level, the refraction may range from — 1.5 D to + 3.0 D. The norm for myopia being — 0.5 D and that for hypermetropia + 0.75 D. At the 6/9 level, the refraction range was from — 2.5 D to + 4.5 D. The norm for myopia being — 0.75 D and that for hypermetropia + 1.5 D. The inaccuracy of visual require-

TABLE III — *The limits of refractive errors encountered together with the mean and modal refraction at each visual acuity level*

Visual Acuity	Myopic limit	Hyper metropic limit	— Error		+ Error	
			Mean	Mode	Mean	Mode
6/5	— 0.5D	+ 2.5D	— 0.25D	— 0.25D	+ 0.75D	+ 0.75D
6/6	— 1.5D	+ 3.5D	— 0.50D	— 0.50D	+ 0.80D	+ 0.75D + 1.0 D
6/9	— 2.5D	+ 4.5D	— 1.0 D	— 0.75D	+ 1.24D	+ 1.25D + 1.5 D

ments in terms of visual acuity alone without considering the refraction becomes evident. Diamond<sup>10</sup> recommends that the requirement for airline pilots should be 6/6 vision with a refraction of not less than + 0.5 D to neutralise the myopia shift of the 20–30 year range and not more than + 1.0 D to offset any deterioration that might occur due to the pre presbyopic hypermetropic shift. This will safeguard against the loss of experienced pilots due to acquired visual defects and will ensure a high standard of visual efficiency over a 10 to 15 year period. This however is an ideal requirement; a more practical approach demands further investigation to widen these limits.

#### DEPTH PERCEPTION AND OCULAR MUSCLE BALANCE

No aspect of vision in aviation has been more extensively investigated and has led to more diversity of opinion than depth perception and its relation to ocular muscle balance. Experience in World War I showed that 70 to 80% of accidents were due to bad landings and according to Clements<sup>7\*</sup> these were mainly caused by heterophoria made manifest by fatigue. Howard<sup>1, 18, 19</sup> in an analysis of World War I accidents concluded that the judgement of distance was mainly dependent on good and equal vision in the two eyes and that the main factor was binocular parallax. This observation resulted in the Howard Dolman test which has ever since been used as a criterion for the depth perception ability necessary for flying. Ocular muscle imbalance was viewed with concern and Doyne<sup>11</sup> held that heterophoria often implied the unequal action of the extra ocular muscles resulting in a bilateral visual disharmony. He considered a one-eyed man with acquired stereoscopic vision less dangerous for flying than a two-eyed man whose eyes may be unreliable. These views resulted in very stringent standards for heterophoria being laid down at the Peace Convention in 1917 and agreed on for international use by the medical sub-committee of the International Commission for Air Navigation at Rome in 1927. These prevailed up to the beginning of World War II.

In the Royal Canadian Air Force, from August, 1942 to October, 1944, 21.7% of candidates were rejected for ocular defects, at the recruiting centres, 4.5% were rejected for ocular muscle balance (Nicholls)<sup>26, 27</sup> The need was, therefore, felt to determine the validity of the ocular muscle balance requirements. On evaluation, it was felt that binocular factors were of greatest value at relatively close range, and it was realised that some functions of depth perception, such as, the estimation of air speed and the determination of the effective range for gunfire were aided by mechanical devices, such as the air speed indicator, and the gunsight, thereby limiting the use of binocular factors in flying. This resulted in the adoption of more liberal standards in the Royal Canadian Air Force, demanding relatively lenient standards for new trainees and not requiring good binocular vision in experienced personnel with good flying records. When Kirschberg's<sup>22</sup> careful study in 1944 found no relationship between heterophoria, fusion, stereoptic acuity and flying performance, this approach was justified.

Various studies Berens<sup>2</sup>, Duguet<sup>12</sup>, Macfarland<sup>23, 24</sup>, Neely<sup>5</sup>, Velhagen<sup>26</sup> on the effect of motion on ocular muscle balance supported these revised standards, in so far as, stereopsis remained very resistant to the effect of motion, though the lateral phorias tended to increase and the convergence weakened. Moreover, since the adverse effects of motion were offset by the use of oxygen and with the advent of pressurised fuselages, ocular muscle balance limitations became unnecessary.

Nicholls<sup>8</sup> classified pilots into four distinct groups according to their ocular muscle balance and their landing capabilities.

*Group I* Pilots with good ocular muscle balance, and who are good landers — the traditional ideal.

*Group II* Pilots with good ocular muscle balance but who are poor landers — the cause lies with the faulty interpretation of the information obtained from the eyes.

*Group III* Pilots with poor ocular muscle balance and who are good landers. These pilots have developed accurate monocular depth perception based on size, motion parallax and perspective.

*Group IV* Pilots with poor ocular muscle balance and who are poor landers. This group comprises only 1% of all pilots and has two sub-divisions —

(a) Good pilots who lose confidence due to stress or some minor flying accident. These benefit by rest and psychotherapy.

(b) Pilots who have never learnt to use monocular cues in landing. These may be helped by orthoptic exercises.

Based on these concepts, Nicholls<sup>28</sup> recommended that providing there is no frank diplopia there is no need for ocular muscle

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<b>DE OCAMPO G, ESPIRITU, R B and SALCEDA SALVADOR R</b> (Philippines) Are the non cellular portions of the cornea viable?	1248
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balance restrictions for pilot duty, and that imbalance of longstanding resulting in neglect or suppression may be acceptable for flying. This last is an extreme view and is controversial. A pilot, with ocular neglect is restricted to a monocular field thereby limiting his chances of target detection. Moreover, since motion parallax is a function of the peripheral retina the effect of the unequal temporal and nasal fields of monocular vision on motion parallax whilst landing should be fully evaluated before accepting this handicap.

The evaluation of a single depth perception factor, as is done by the depth perception tests in current use, is not valid to assess or predict the complex function of spatial orientation. The use of these tests as criteria of potential flying performance is not justified. There is also no doubt that binocular cues are of little value as aids to flying. Teichner and his co-workers<sup>28</sup> find that they are slightly superior to the monocular cues only up to 1900 ft. Rose<sup>29</sup> and Scobee<sup>31</sup> also find binocular cues widely overrated since the pilot's visual tasks are performed at distances at which binocularity makes little difference. Evaluating the monocular cues Rose<sup>29</sup> finds that motion parallax and the size of retinal image are the main factors during flight and landing. Cabis<sup>8</sup> finds linear perspective and the size of retinal image most important cues and that flying ability can be improved by training and does not rely upon a well developed sense of stereopsis.

The piloting of aircraft through periscopes and closed circuit television is envisaged. The problems attendant with this procedure are the maintenance of the convergence accommodation ratio, the effect on distance judgement, of instrument magnification, of the scope haze and of the apparent increase in the angular velocity of approaching objects caused from the difference between the pilot's eye position and the objective.

In laying down standards there is a tendency to assume that if ocular muscle balance is normal it follows that the depth perception is adequate to meet the demands of flying. Experience in the Indian Air Force justifies this view. It is probable that the poor landers of Nicholls' Group II and IV are either eliminated at the training stage or improve their depth perception as training and experience proceed.

In Indian Air Force the limits of heterophoria are 6.0 p.d. of esophoria and exophoria and 1.0 p.d. of hyperphoria at 6 meters and 6.0 of esophoria 16.0 p.d. exophoria and 1.0 p.d. hyperphoria at 30 cms. The main reason for these limitations is to ensure against decompensation in flight from fatigue and flying stresses. With this object in view, the main weightage in routine ocular muscle balance tests for flying fitness should be given to the tests that evaluate the fusion sense. In a review of ocular muscle balance tests performed on candidates for the Indian Air Force,<sup>31</sup> the incidence of the lateral phorias as determined by the Maddox Rod at 6 meters and 30 cms in 775 cases reviewed is indicated in Fig. 2.



In the Royal Canadian Air Force, from August, 1942 to October, 1944, 21.7% of candidates were rejected for ocular defects, at the recruiting centres, 4.5% were rejected for ocular muscle balance (Nicholls)<sup>26, 28</sup>. The need was, therefore, felt to determine the validity of the ocular muscle balance requirements. On evaluation, it was felt that binocular factors were of greatest value at relatively close range, and it was realised that some functions of depth perception, such as, the estimation of air speed and the determination of the effective range for gunfire were aided by mechanical devices, such as the air speed indicator, and the gunsight, thereby limiting the use of binocular factors in flying. This resulted in the adoption of more liberal standards in the Royal Canadian Air Force, demanding relatively lenient standards for new trainees and not requiring good binocular vision in experienced personnel with good flying records. When Kirschberg's<sup>29</sup> careful study in 1944 found no relationship between heterophoria, fusion, stereoptic acuity and flying performance, this approach was justified.

Various studies Berens<sup>3</sup>, Duguet<sup>1</sup>, Macfarland<sup>3, 24</sup>, Neely<sup>5</sup>, Velhagen<sup>36</sup> on the effect of anoxia on ocular muscle balance supported these revised standards, in so far as, stereopsis remained very resistant to the effect of anoxia, though the lateral phorias tended to increase and the convergence weaken. Moreover, since the adverse effects of anoxia were offset by the use of oxygen and with the advent of pressurised fuselages, ocular muscle balance limitations became unnecessary.

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In Indian Air Force the limits of heterophoria are 5.0 p.d. of esophoria and exophoria and 1.0 p.d. of hyperphoria at 6 meters and 6.0 of esophoria, 16.0 p.d. exophoria and 1.0 p.d. hyperphoria at 30 cms. The main reason for these limitations is to ensure against decompensation in flight from fatigue and flying stresses. With this object in view, the main weightage in routine ocular muscle balance tests for flying fitness should be given to the tests that evaluate the fusion sense. In a review of ocular muscle balance tests performed on candidates for the Indian Air Force<sup>21</sup> the incidence of the lateral phorias as determined by the Maddox Rod at 6 meters and 30 cms in 775 cases reviewed, is indicated in Fig. 2.

Fig. 2

Distribution of the lateral phorias at 6 m and 30 cms (775 cases)

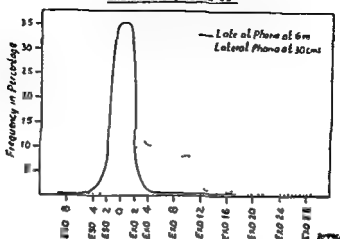


FIG. 2

Distribution of the lateral phorias at 6 m and 30 cms (775 cases)

The curve of the lateral phorias at 6 meters shown are approximately normal distribution, peaking at 0.5 pd of esophoria and exophoria—80.2% falling between 1.5 pd of esophoria and 1.5 pd of exophoria. The curve for lateral phoria at 30 cms shows an uneven distribution, but (84.7%) fall between 1 pd and 10 pd of exophoria, indicating a shift towards exophoria at near distance. This is because any deficit of the convergence required at 30 cms is manifested as an exophoria, (and so explains the very frequent association of bar responses in the Bishop Harman test and latent divergence on the near cover test with moderate esophoria at near distance). In no instance, did the Maddox rod tests give any indication of uniocularity, this was only revealed by the Bishop Harman and cover tests.

Comparative values of objective convergence (C), subjective convergence (SC), and the SC—C difference in borderline and unfit cases are shown in Table IV.

TABLE IV — Average convergence values in borderline and unfit cases

	No	Obj Con (C) in cms	Subj Con (SC) in cms	SC—C in cms
Binocular cases beyond Maddox rod limits	15	7.4	15.7	8.3
Unocular cases				
(a) beyond Maddox rod limits	8	7.7	21.0	13.3
(b) within Maddox rod limits	12	8.0	18.8	10.8

It is evident that the larger SC—C differences are associated with unilocularity, and therefore the SC—C difference gives a good indication of the fusion sense. The smaller the difference the better the fusion; the larger differences, especially when associated with higher C values indicate poor fusion. This is worthy of confirmation by further investigation since the test is a simple one requiring simple equipment and little skill.

In our experience there has been no known case of a decompensation of heterophoria among aircrew, either from flying stresses or from any other reason. The range of lateral phorias in 206 Air Force and air line pilots is shown in Table V.

TABLE V — Mean and Range of Lateral Phoria Values in serving aircrew (206)

	Far	Near
Mean	0.03 p.d. Eso	5.69 p.d. Exo
95% range	2.0 p.d. Eso to 4.0 p.d. Exo	6.0 p.d. Eso to 16.0 p.d. Exo
Total Range	8.0 p.d. Eso to 18.0 p.d. Exo	8.0 p.d. Eso to 24.0 p.d. Exo

The extreme limit of exophoria 18 p.d. for far and 24 p.d. for near is represented by an airline pilot who is unilocular on the Bishop Harman with the cover test indicating alternating divergence, who was initially made fit when examining conditions were more lax. He now has a good flying record of more than 5000 hours to his credit.

#### SUMMARY AND CONCLUSION

The piloting of high speed aircraft at high altitude demand a high degree of uncorrected visual acuity. The visual standards prevalent in the Indian Air Force of 6/6-6/9 vision meets these requirements ensuring a binocular visual acuity of 6/5 in (79-80%) of the population accepted a refraction range, from +0.5 to +1.5 D in 80% of serving pilots which suits search under empty visual field conditions and which is a safeguard against the loss of visual efficiency due to acquired defects.

It would be more accurate to combine the visual acuity level with limits of refraction. The ideal range of refraction acceptable for initial trainees would be +0.5 D to +1.0 D, but to be practical, wider limits should be considered. It would be advantageous to establish criteria for speedy visual perception in personnel assigned to high performance aircraft.

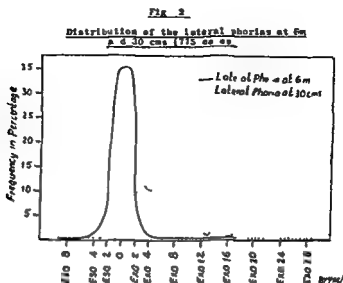


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It is evident that the larger SC—C differences are associated with unimolarity, and therefore the SC—C difference gives a good indication of the fusion sense. The smaller the difference, the better the fusion, the larger differences especially when associated with higher C values indicate poor fusion. This is worthy of confirmation by further investigation since the test is a simple one requiring simple equipment and little skill.

In our experience there has been no known case of a decompensation of heterophoria among aircrew, either from flying stresses or from any other reason. The range of lateral phorias in 206 Air Force and air line pilots is shown in Table V.

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Total Range	8.0 p.d. Eso	8.0 p.d. Eso
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The extreme limit of exophoria 18 p.d. for far and 24 p.d. for near is represented by an airline pilot who is unocular on the Bishop Harman with the cover test indicating alternating divergence, who was initially made fit when examining conditions were more lax. He now has a good flying record of more than 5 000 hours to his credit.

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It would be more accurate to combine the visual acuity level with limits of refraction. The ideal range of refraction acceptable for initial trainees would be +0.5 D to +1.0 D but to be practical wider limits should be considered. It would be advantageous to establish criteria for speedy visual perception in personnel assigned to high performance aircraft.

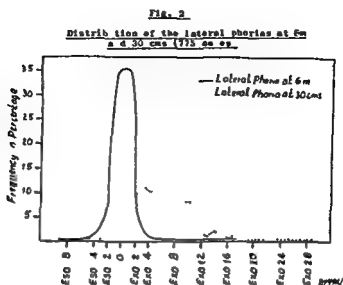


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#### SUMMARY AND CONCLUSION

The piloting of high speed aircraft at high altitude demand a high degree of uncorrected visual acuity. The visual standards prevalent in the Indian Air Force of 6/6–6/9 vision meets these requirements by using a binocular visual acuity of 6/5 in (79–8%) of the population. Accepted a refraction range, from +0.5 to +1.5 D in 80% of serving pilots which suits search under empty visual field conditions and which is a safeguard against the loss of visual efficiency due to acquired defects.

It would be more accurate to combine the visual acuity level with limits of refraction. The ideal range of refraction acceptable for initial trainees would be +0.5 D to +1.0 D but to be practical wider limits should be considered. It would be advantageous to establish criteria for speedy visual perception in personnel assigned to high performance aircraft.



A very fine degree of depth perception is required to land high speed aircraft. This ability bears no relation to heterophoria, nor can it be evaluated by any single depth perception test, it can be improved by training. The most important monocular cues in flight and landings are motion parallax, retinal image and linear perspective.

Though binocular cues only operate at limited distances, good binocular vision is necessary to provide a potentially wider visual field for target detection and for visual tasks within the cockpit, such as the efficient viewing of C.R.T. displays. Hence, the main objective of the ocular muscle examination of aircrew should be to establish the presence of binocularity with good fusion to ensure against decompensation in the face of flying stresses.

Of the routine ocular muscle balance tests, only the Bishop Harman test and the cover test reveal unocular tendencies, and that the difference between the subjective and the objective convergence is an excellent indication of the quality of the fusion sense. In the evaluation of flying fitness, if due weightage is given to these tests, the ocular muscle balance requirements for modern flying will be fully met.

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## EALES'S DISEASE—HISTORICAL REMARKS

M J ROPER HALL

*Birmingham England*

Henry Eales was born in 1852—25 years later in 1877 he was appointed surgeon at the Birmingham Eye Hospital and in 1880, published a paper in the Birmingham Medical Review entitled 'Cases of retinal haemorrhage associated with epistaxis and constipation' The following year he read a paper on the same subject of primary retinal haemorrhage in young men at the International Medical Congress in London

At the end of his career he was described as a man of singularly amiable character to whom his colleagues were sincerely attached He died in 1913 while holding the appointment of Senior Surgeon to the Birmingham Eye Hospital In his obituary notices attention was drawn to his publications on the state of the retina in 100 cases of granular kidney on unocular retinitis albuminurica, on toxic amblyopia on causes and treatment of convergent squint and on paralysis of convergence and accommodation but no mention was made of his papers on the disease which bears his name and which forms the subject of the Symposium at this International Congress

### CLINICAL FINDINGS

In his two papers on this subject he makes the points that the left eye was primarily and chiefly affected that vitreous haemorrhage is recurrent the vessels of the retina are found to be large and tortuous especially the veins that the haemorrhages were usually confined almost entirely to the periphery of the retina only occasionally being found round the disc and the macular area was not involved in any case The extravasations were almost invariably large, round or irregular and could often be seen to have proceeded from venous radicles which were obscured by them All his cases were young men between 14 and 20 years of age all had been subject to epistaxis especially during the Summer months, and all had been much troubled with constipation for some two to three years In all cases the pulse was habitually under 60 per min, but easily excited to rapidity In acknowledging the rarity of the condition he pointed out that by chance some four cases had come to his attention within a short period and that in the following year—although 12 000 out patients were treated at our hospital—not a single fresh case was seen He considered it remarkable that no case had been seen in a female and wondered whether the menstrual function was a safeguard

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# LES PROBLEMES OPHTALMOLOGIQUES POSES PAR L'ENVIRONNEMENT AU COURS DU VOL SPATIAL

A MERCIER<sup>1</sup> et G. PERDRIEL<sup>2</sup>

(Tours France)

Quittant la terre pour l'espace l'astronaute enfermé dans une capsule, se trouve transporté dans un milieu nouveau auquel son organisme doit s'adapter. De même que toutes ses fonctions sensorielles, sa vision subira les effets de cet environnement inhabituel qui en médecine de l'espace, constitue l'agent stressant principal.

Nous avons utilisé pour cette étude les renseignements recueillis lors des vols des cosmonautes américains et soviétiques.

Nous envisagerons successivement l'influence sur la fonction visuelle de deux sortes d'environnement :

- 1 l'environnement extérieur à la capsule
- 2 l'environnement intérieur à la capsule
- 1 l'environnement extérieur

Les accélérations qui surviennent lors de la mise à feu de la fusée porteuse atteignent des taux susceptibles d'altérer la vision. Lors des vols de Shepard et Grissom l'accélération de départ passa de 1 G à 6,3 G en 2 minutes, elle fut de 6,7 G dans le vol de Glenn pour atteindre 7,7 G dans les 2 minutes suivantes. Aucune altération visuelle ne fut signalée à cette occasion.

Par contre les vibrations qui lors du vol de Shepard apparurent une minute après le lancement et au passage de la zone transsonique provoquèrent l'entrée en vibration de la tête de l'astronaute dont la vision fut momentanément brouillée, les aiguilles des cadrans de bord ayant une apparence floue. Ce trouble fut de très courte durée, car 125 m après le lancement Shepard était capable de lire et de transmettre au sol les indications concernant la pression à l'intérieur de la cabine. Des perfectionnements techniques ont d'ailleurs réduit la fréquence et l'amplitude de ces vibrations lors des vols suivants et fait disparaître leur repercussion sur la vision.

C'est lors de la ré-entrée dans l'atmosphère que les forces d'accélération atteignent leur valeur maxima en passant de 0,05 à 11 G en 31 secondes. A ce moment les fonctions visuelles demeurèrent normales et les cosmonautes n'éprouvèrent pas de réduction du champ

<sup>1</sup> Chairman of the Vision Committee, Aero Space Medical Panel, AGARD, NATO

<sup>2</sup> Médecin Commandant, Professeur Agrégé de Service de Santé de l'Air

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## 1 l'environnement extérieur

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visuel peripherique ni de "grav-out". De meme, lors du deploiement du parachute, une pointe a  $4\text{ G}$  n'entraîna aucun trouble visuel. Les accelerations lineaires de depart et de re-entree n'ont donc, au point de vue oculaire, rien provoqué de plus que les reactions constatees lors des essais en centrifugeuse pour des valeurs de  $G$  correspondantes.

Le vol spatial introduit la notion de la 3eme dimension de l'espace et l'astronaute doit pouvoir controler non seulement l'altitude, mais egalement le profil vertical et l'orientation geographique. Les rotations successives de la capsule au cours du vol et les types inhabituels d'accelerations angulaires agissant a la fois sur la vision et les canaux semi-circulaires peuvent provoquer la *desorientation*. C'est ainsi que Grissom a pu eprouver une breve sensation de chute lors de la separation de la fusée porteuse et le sentiment de filer en arriere a la mise a feu des retro-fusees. L'entrainement qui a educé l'astronaute a ne plus accorder foi qu'aux seules indications de ses instruments en negligeant ses propres sensations visuelles et cenesthetiques, semble avoir considerablement atténue sinon supprime cette cause d'erreur humaine.

La pesanteur peut etre considerée comme le principal element de l'environnement exterieur car notre corps, au point de vue anatomique et physiologique, est, dans la vie terrestre, constamment controlé par la pesanteur. Or, au cours du vol spatial, lorsque la force d'attraction de la terre est contrebalancée par la force centrifuge du vehicule, il en resulte un etat de sub puis d'apesanteur qui modifie complètement notre equilibre habituel.

L'etude du comportement de l'homme en l'absence de pesanteur a tout d'abord donne lieu a de nombreuses experiences preliminaires rendues difficiles du fait de difficulte de realiser artificiellement a proximité de la terre la suppression de la pesanteur pendant un certain laps de temps. Les constatations faites lors des vols de  $1 \times 15$ , les experiences de Whiteside sur un sujet immergé, ont indique que l'homme manifestait une incoordination psycho-motrice transitoire lors du passage d'un taux eleve de  $G$  a  $0\text{ G}$ . Whiteside a fait montre que, lorsque la valeur de  $G$  passait de  $1$  a  $0$ , l'objet fixe par le sujet semblait etre plus bas qu'en realite alors qu'au contraire l'objet semblait s'elever par rapport au sujet pour une valeur de  $2\text{ G}$ . Dans un film sovietique realise lors de l'envoi d'un chien dans une fusée spatiale, Kousnetsov a pu constater, lors du passage en apesanteur, la deviation vers le bas des yeux de l'animal dont la tete avait été maintenue immobile en la fixant avec du platre.

Il est possible qu'une alteration du tonus musculaire soit a l'origine de ces deviations. Les auteurs sovietiques (S. V. Ugan) ont en effet indique que si l'on mesure la force musculaire d'un sujet en etat de pesanteur puis d'apesanteur, on le voit souvent passer de  $45/60\text{ kgs}$  a  $4/5\text{ kgs}$ .

L'analyse des mouvements des yeux de Shepard enregistres par la camera placee dans la capsule a permis de verifier si, durant les



diverses phases du vol, son attention s'était toujours dirigée correctement vers les instruments qu'il devait contrôler.

C'est ainsi que, pendant les 20 premières secondes il regarda la zone 9 du tableau de bord où se trouvaient les signaux lumineux indiquant le bon fonctionnement du lancement ou l'obligation d'éjecter la capsule (Ready or Mayday). Durant le reste de la période de lancement son regard observa les différentes zones contenant les indications concernant l'altitude, l'accélération, le tangage, la pression, la cabine, le carburant et l'oxygène. Durant la pesanture, les zones 6, 7, 8 furent les plus observées (Attitude de la capsule, heure periscope). Lors de la rentrée, le regard fut surtout fixé sur la zone 4 contrôlant l'accélération durant la phase de la plus forte valeur de  $G$  et la zone 8 contenant le periscope qui servit à vérifier le bon développement du parachute.

Ce film a démontré qu'en toutes circonstances et notamment durant l'absence de pesanture, le regard fut toujours correctement dirigé sur les instruments appropriés sans qu'il apparaisse aucune trace d'incertitude ou d'incoordination dans les mouvements oculaires, de fixité intempestive ou de nystagmus. L'astronaute put toujours effectuer en temps voulu les divers mouvements commandés par les indications perçues visuellement sur le tableau de bord.

Les renseignements recueillis lors du vol de Shepard, dont le séjour en apesanture n'a guère dépassé 5 minutes, ont été confirmés par les vols suivants de Glenn (4 heures 30 d'apesanture), Titov (25 heures) et enfin Popovich (71 heures) et Nicolaïev (94 heures). L'absence de pesanture ne provoque pas de troubles visuels. Les observations spéciales faites à ce sujet par Glenn à l'aide d'optotypes et d'un oculogyrisc test ont prouvé que la vision et la motilité oculaire demeuraient normales.

Bien que la capsule spatiale soit hermétiquement close, un hublot permet l'observation extérieure en dehors du periscope. Lorsque la rotation de la capsule dirige cette ouverture en direction du soleil, l'éblouissement devient intense. Cet éblouissement est d'autant plus vif qu'en très haute altitude le bleu du ciel devient de plus en plus sombre. Les travaux de White, Riley et Jorve ont montré que la lecture des instruments de bord était influencée par l'association de l'éblouissement et de l'accélération. Au taux le plus élevé de brillance (42 milli lambert) il n'existe pas de différence dans le pourcentage d'erreurs commises aux différentes valeurs de  $G$ . Au taux de brillance le plus bas, la fréquence des erreurs est en raison inverse de la brillance et en rapport direct avec la valeur de  $G$ . À  $4G$ , il y a une augmentation systématique du pourcentage d'erreurs lorsque la brillance diminue.

Si tous les astronautes américains ou soviétiques ont signalé l'éblouissement intense survenant lors de l'exposition du hublot en direction du soleil, aucune indication n'a été donnée concernant la perturbation visuelle ayant pu en résulter à part les fréquentes modifications de l'adaptation rétinienne.

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L'analyse des mouvements des yeux de Shepard enregistres par la camera placee dans la capsule a permis de verifier si, durant les

et du vêtement qui est d'environ 14,7 livres par square inch lors du lancement passe à 5,7 après une minute et demie et est maintenu à ce taux pendant toute la durée du vol jusqu'à une reprise de la pressurisation à 25 000 pieds lors de la descente après ouverture des parachutes.

La température à l'intérieur de la cabine et du vêtement doit être également maintenue à des taux permettant un bon équilibre physiologique. Elle varie d'environ 15° lors du départ et de la descente et aurait été maintenue entre 14° et 24° C (58° F et 76° F) pendant toute la durée des vols de Nikolaïev et Popovich. Glenn cependant se plaignit d'une transpiration abondante durant les dernières phases de sa descente et de sa récupération.

L'humidification de l'air dans la capsule joue un rôle aussi important que la température étant donné les relations qui existent entre ces deux éléments. C'est ainsi que l'addition d'une humidité de 10% à une température sèche de 70° F fait passer cette dernière à 63° F et qu'une humidité de 70% produit, pour la même température sèche de 70° F un abaissement à 67° F. Les expériences préliminaires aux divers vols spatiaux avaient montré que la température ne devait pas dépasser 90 à 95° F (32 à 35° C) pour permettre l'exécution normale des diverses tâches incombant à l'astronaute.

Le souci d'éviter les erreurs que pourraient provoquer des perturbations oculomotrices du fait des accélérations ou de la pesanteur a fait répartir les multiples cadrans et instruments de bord de façon à réduire l'amplitude des mouvements oculaires du pilote. L'analyse du film de Shepard avait en effet montré qu'étant donné la fréquence du regard entre l'indicateur de G et celui de carburant, il était indispensable de réduire la distance séparant ces deux cadrans.

Les gaz nocifs depuis l'oxyde de carbone jusqu'aux fumées et vapeurs irritantes peuvent avoir une influence nocive sur la vision, mais c'est là un problème que les ingénieurs ont su résoudre en réalisant de véritables circuits régulateurs à l'intérieur du vêtement et de la capsule tant pour l'oxygénation et l'épuration de l'air que pour sa température et son humidification.

Mais les facteurs psycho-somatiques semblent être au moins aussi importants en ce qui concerne l'environnement intérieur.

Dès le moment où l'astronaute pénètre dans la capsule, il est isolé du monde extérieur. Certes, il demeurera en relation radio-phonique avec la terre durant la durée du vol, mais l'isolement et le confinement l'attendent d'un départ dont on ne peut presumer la réussite constituent à n'en pas douter une rude épreuve morale. Je me souviens d'avoir entendu Yeager, un des premiers pilotes de l'avion expérimental X, dire que le moment le plus pénible était celui où, enfermé dans son avion fusée, il attendait, inactif d'être largué du bombardier qui le transportait en altitude. Or, dans certains cas, il s'écoula plusieurs heures entre l'insertion de l'astronaute dans la capsule et la mise à feu de la fusée porteuse. L'appréhension

Ce que l'on a appelé *l'environnement meteorologique* a suscite de nombreuses recherches avant l'envoi du premier homme dans l'espace. En effet, si la composition de l'atmosphere au niveau de la mer est favorable a l'homme, car sa densite constitue un écran protecteur contre les radiations ionisantes et les meteorites, plus on s'eloigne de la terre, plus le milieu environnant devient hostile.

En pratique, on sait que les radiations primaires composees de protons (79%), de particules alpha (20%), et de noyaux lourds (1%), traversant l'atmosphere a l'altitude de 60 a 70 000 pieds, transmettent leur energie aux composantes de cette atmosphere en produisant des radiations secondaires, qui, peu a peu, se transforment en chaleur. Les effets nocifs des radiations primaires augmenteront avec l'altitude, les noyaux les plus lourds apparaissant surtout au dessus de 60 000 pieds. Leur influence sur l'organisme, et principalement sur les organes visuels ne paraît pas devoir entrainer de troubles graves car il a été calculé qu'un pilote volant pendant 30 ans à une altitude de 75 000 pieds ne serait expose qu'à une quantité totale de 108 r C M (Roentgen equivalent man). Enfin, les auteurs soviétiques n'auraient constate qu'un taux de 10 millirad à l'interieur des visseurs cosmiques et les animaux places dans les fusées experimentales n'auraient pas presente de modifications biologiques importantes.

L'integrite fonctionnelle du vehicule et les systemes de protection prevus mettent pratiquement l'astronaute a l'abri des eventuels effets nocifs des radiations ionisantes, tout au moins pour les altitudes atteintes jusqu'à ce jour.

## 2 L'ENVIRONNEMENT INTERIEUR

Isole dans une étroite capsule, couche sur un siege moule d'après son corps, emprisonné dans un vêtement pressurisé truffé d'électrodes, la tête enfermée dans un scaphandre, l'astronaute se voit transféré dans un véritable "no man's land" où il va se trouver en presence de responsabilites que tous les entraînements antérieurs risquent de n'avoir pas toujours établi de façon précise.

Cet environnement interieur comporte donc des facteurs physico-physiologiques et psycho-somatiques susceptibles de retentir sur la vision.

Parmi les premiers, *l'oxygenation* joue un rôle important, car il n'est pas besoin de rappeler les effets de l'anoxie sur la perception visuelle. Une oxygenation de 100% est realisée depuis la fermeture de la capsule au debut du count down et durant tout le vol. Ce n'est que lorsque l'altitude de 25 000 pieds est atteinte lors de la descente que l'ouverture de valves permet l'entree de l'air dans la cabine étanche. Une analyse de l'air de la capsule apres une d'oxygenation a 100% a montre qu'il existait un taux de 90% d'oxygene.

Le maintien d'une pression correcte à l'interieur de la cabine et du vêtement est également très important pour le bon fonctionnement de toutes les fonctions sensorielles. Le taux de pression de la cabine



et du vêtement qui est d'environ 14,7 livres par square inch lors du lancement passe à 5,7 après une minute et demie et est maintenu à ce taux pendant toute la durée du vol jusqu'à une reprise de la pressurisation à 25 000 pieds lors de la descente après ouverture des parachutes.

La température à l'intérieur de la cabine et du vêtement doit être également maintenue à des taux permettant un bon équilibre physiologique. Elle varie d'environ 15° lors du départ et de la descente et aurait été maintenue entre 14 et 24° C (58° F et 76° F) pendant toute la durée des vols de Nikolaïev et Popovich. Glenn cependant se plaignit d'une transpiration abondante durant les dernières phases de sa descente et de sa récupération.

L'humidification de l'air dans la capsule joue un rôle aussi important que la température étant données les relations qui existent entre ces deux éléments. C'est ainsi que l'addition d'une humidité de 10% à une température sèche de 70° F fait passer cette dernière à 63° F et qu'une humidité de 70% produit pour la même température sèche de 70° F un abaissement à 67° F. Les expériences préliminaires aux divers vols spatiaux avaient montré que la température ne devait pas dépasser 90 à 95° F (32 à 35° C) pour permettre l'exécution normale des diverses tâches incombant à l'astronaute.

Le souci d'éviter les erreurs que pourraient provoquer des perturbations oculomotrices du fait des accélérations ou de la pesanteur a fait repartir les multiples cadrans et instruments de bord, de façon à réduire l'amplitude des mouvements oculaires du pilote. L'analyse du film de Shepard avait en effet montré qu'étant donnée la fréquence du regard entre l'indicateur de G et celui de carburant, il était indispensable de réduire la distance séparant ces deux cadrans.

Les gaz nocifs depuis l'oxyde de carbone jusqu'aux fumées et vapeurs irritantes, peuvent avoir une influence nocive sur la vision, mais c'est là un problème que les ingénieurs ont su résoudre en réalisant de véritables circuits régulateurs à l'intérieur du vêtement et de la capsule tant pour l'oxygénation et l'épuration de l'air que pour sa température et son humidification.

Mais les facteurs psychosomatiques semblent être au moins aussi importants en ce qui concerne l'environnement intérieur.

Dès le moment où l'astronaute pénètre dans la capsule, il est isolé du monde extérieur. Certes, il demeurera en relation radio-phonique avec la terre durant la durée du vol, mais l'isolement et le confinement, l'attente d'un départ dont on ne peut presumer la réussite constituent à n'en pas douter une rude épreuve morale. Je me souviens d'avoir entendu Yeager, un des premiers pilotes de l'avion expérimental X, dire que le moment le plus pénible était celui où, enfermé dans son avion fusée, il attendait inactif d'être largué du bombardier qui le transportait en altitude. Or, dans certains cas, il s'écoula plusieurs heures entre l'insertion de l'astronaute dans la capsule et la mise à feu de la fusée porteuse. L'appréhension

l'anxiété, si l'on ne veut pas parler de la peur, cependant bien naturelle en de telles circonstances, ont sur les processus mentaux supérieurs, et par voie de conséquence sur la vision, une influence non négligeable.

Si les pilotes de jets ressentent parfois, à très haute altitude, le "break off" préjudiciable à l'intégrité visuelle, l'astronaute doit se trouver encore plus séparé de la terre qu'il n'apercevra par instants, que sous l'apparence d'un fragment de mappemonde. Heureusement, la multiplicité de ses tâches ne lui laissent pas le temps d'épiloguer sur sa situation pour le moins anormale. La surveillance des instruments, la fréquence des indications qu'il doit transmettre au sol l'obligent à une attention soutenue. Mais l'homme ne peut travailler intensément de façon continue que pendant des périodes relativement courtes s'il ne veut pas être enclin à l'erreur et devenir inapte à remplir sa mission. C'est la raison pour laquelle, lors des vols soviétiques de longue durée, les astronautes durent consacrer au sommeil une partie de leur temps (8 heures sur 25 dans le cas de Titov).

Le vol spatial demande donc de l'adresse, de l'intelligence et un remarquable "self control". L'environnement extérieur et intérieur qui situe l'astronaute en un milieu nouveau auquel son corps n'est pas adapté, l'expose à une succession de stresses susceptibles d'altérer le bon fonctionnement de ses fonctions sensorielles et de ses processus mentaux. En effet, la capacité du système nerveux central d'interpréter et de réaliser l'information transmise par les récepteurs sensoriels demeure à la base de l'efficacité humaine, et, en dépit de toutes les expériences effectuées en laboratoire pour déterminer, au point de vue visuel, le temps requis par la perception, l'intégration, la décision et la réaction en connection avec les problèmes particuliers survenant au cours de tels vols, il était permis de supposer que les chocs physiologiques et les émotions étaient susceptibles d'aggraver l'anisochronie psychosensorielle.

Il semble bien qu'il n'en ait rien été.

L'entraînement à certainement joue un rôle capital en mettant artificiellement le futur astronaute dans des conditions très proches de celles auxquelles il allait être soumis en vol, et en lui apprenant ce qu'il devait regarder et ce qu'il devait exécuter en toutes circonstances. La sélection et un entraînement intensif, joints à la perfection des installations techniques ont donc permis aux diverses astronautes d'effectuer sans retentissement préjudiciable à leurs fonctions visuelles les vols spatiaux réalisés jusqu'à ce jour. Et si leurs expériences ont prouvé l'efficacité de cette indoctrination préalable, elles ont aussi démontré l'aptitude, assez inattendue, de l'organisme humain à s'adapter à des conditions de vie totalement différentes de celles pour lesquelles il a été conçu.

## LE CHAMP VISUEL EN ALTITUDE

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Les observations faites sur le champ visuel au cours des vols astronautiques sont actuellement gardées secrètes aussi ne peut il être question de se reporter à une étude bibliographique L'expérimentation étant d'autre part inaccessible, il n'est pas possible de donner la moindre précision dans ce domaine Notre propos sera plus modeste et nous nous contenterons de rapporter ce que nous connaissons des vols « haute altitude » à la lumière de la littérature et des expériences que nous avons pu effectuer Les modifications du champ présentent non seulement un intérêt pratique qui pourra sans doute être appliqué aux vols cosmiques mais aussi un intérêt physiologique

Les variations constatées proviennent de l'anoxémie des changements de pression des accélérations parfois d'autres causes comme l'éblouissement du aux modifications de l'ambiance lumineuse Les plus connues sont celles qui sont dues à l'anoxémie et aux pressions car elles peuvent être facilement étudiées en caisson

### 1 — DEPRESSION ANOXEMIE —

Il y a lieu d'étudier successivement les modifications du champ visuel périphérique et celles du champ moyen, surtout dans la région de la tache de Mariotte on peut en principe opposer l'extrême résistance des isoptères normaux du champ en altitude à l'extraordinaire labilité des caractéristiques physiologiques de la région pericæcale

Les avis des auteurs diffèrent quant aux conséquences de l'altitude sur les limites périphériques du champ visuel

En 1918 WILMLR et BERENS sur 20 sujets soumis au caisson constataient entre 1600 mètres et 3200 mètres un élargissement passager et peu important des formes et des couleurs A 4800 m se produisait une contraction périphérique A 6000 m la contraction devenait plus importante et plus nette à la partie inférieure du champ et avait une amplitude de 7° environ Mais la technique n'était pas précisée du point de vue photométrique

GOJDMANN et SHUBERT ont fait des expériences en caisson ainsi que dans des mélanges gazeux pauvres en oxygène Le test était un objet noir sur fond blanc Ils ont observé une contraction de la partie nasale et supérieure du champ visuel vers 4200 mètres Elle était de 15° à l'altitude de 6500 à 7000 mètres les limites temporales étant peu modifiées L'inhalation d'oxygène ramène le champ à ses limites Les auteurs pensent que l'action est réversible



FURUYA, sur six sujets, constate à 5000 mètres une contraction débutant du côté temporal, accentuée par la prolongation du séjour en altitude.

LIVINGSTONE avec le périmètre de CARGILL, en utilisant un test de 2 millimètres de diamètre trouve une contraction du champ pour des altitudes de 4500 à 5800 mètres. Elles sont symétriques et suivies parfois d'une tendance à l'élargissement lorsque le séjour en altitude se prolonge. Au-delà de 10000 mètres, apparaissent des modifications plus nettes attribuées à l'acroembolisme. Nous en reparlerons plus loin.

KARIFLEIS et SEIGERT ont repris les expériences de GOIDMANN et SHUBERT avec des tests blancs sur fond gris foncé. Même à des altitudes supérieures à 7000 mètres, ils n'ont pas trouvé de variations dignes d'être retenues. Elles seraient en effet de l'ordre de 1° à 3°, mais en réalité, leur technique est différente de celle de GOIDMANN. Ils font remarquer qu'il existe une considérable diminution de l'attention en altitude.

Pour MAC FARLAND, ces résultats contradictoires sont dus aux différences des techniques et surtout d'éclaircissement des tests. Il est bien certain que l'on ne peut guère confronter des expériences menées d'une manière aussi diverse, mais les erreurs proviennent surtout, selon nous, de la méconnaissance des fluctuations statistiques normales des limites périmétriques. Des expériences faites en périmétrie cinétique sur l'appareil de GOIDMANN modifié, et muni de dispositifs électroniques, nous avons pu conclure que les réponses présentent au sol une dispersion assez considérable. À la périphérie vers 60°, leur moyenne est de 5°. À la partie centrale, vers 10°, elles peuvent atteindre 10°.

Nous avons sur 15 sujets repris ces expériences en creux, avec un périmètre de GOLDMANN, après mensuration du diamètre pupillaire qui ne varie d'ailleurs pas du fait de l'altitude. Le tracé normal des isoptères par la technique habituelle avec plusieurs combinaisons de surface et d'intensité pour le même isoptère, ne nous a montré aucune différence significative entre le sol, les altitudes de 3500, 4000, 6000 et 7000 mètres. Nous avons alors recherché systématiquement le lieu de perception d'un test donné présenté dans le champ, en allant de la périphérie vers le centre, et nous avons répété l'expérience dix fois pour dessiner le nuage des points obtenus. Au sol la dispersion est de 5° dans le méridien oblique nasal supérieur avec le test de 5/4 à 50°, à 4500 mètres le nuage de dispersion reste le même. L'inspiration d'O<sub>2</sub> ne modifie rien. Avec un test de 3/3 sur le même méridien la dispersion est de 8° entre 30° et 38°, l'altitude de 4500 mètres ou l'inspiration d'O<sub>2</sub> ne changent rien. Il est certain que le fait de ne pas tenir compte de ces dispersions et de leur absence de variation peut faire croire à des différences d'une expérience à l'autre. On peut donc conclure que les isoptères restent remarquablement fixes dans les conditions normales d'altitude. Au-delà, l'acroembolisme modifie considérablement les choses (Fig. 2).

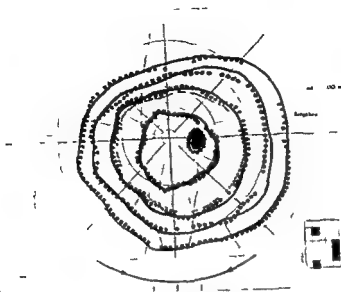


FIG. 1

Isoptères du champ visuel à l'altitude de 3700 m — En traits pleins isoptères au sol  
— En pointillé isoptères en altitude

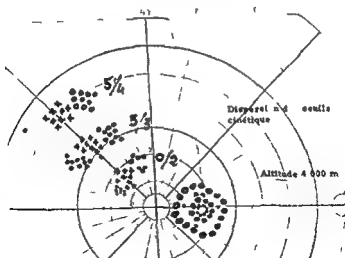


FIG. 2

Dispersion de dix réponses avec les tests 5/4 3/3 et 0/2 Au sol croix — à l'altitude de 4000 m cercles — en altitude sous 0° points noirs Les nuages de points restent les mêmes en vision périphérique Par contre autour de la tache de Mariotte ils s'échelonnent concentriquement pour deux tests différents

FURUYA, sur six sujets, constate à 5000 metres une contraction debutant du cote temporal, accentuee par la prolongation du sejour en altitude

LIVINGSTON avec le perimetre de CARGILL, en utilisant un test de 2 millimetres de diametre trouve une contraction du champ pour des altitudes de 4500 à 5800 metres. Elles sont symetriques et suivies parfois d'une tendance à l'elargissement lorsque le sejour en altitude se prolonge. Au delà de 10000 metres, apparaissent des modifications plus nettes attribuees à l'acroembolisme. Nous en reparlerons plus loin.

KYRIELFIS et SEIGERT ont repris les experiences de GOLDMANN et SHUBERT avec des tests blancs sur fond gris foncé. Même à des altitudes superieures à 7000 metres, ils n'ont pas trouve de variations dignes d'être retenues. Elles seraient en effet de l'ordre de  $1^{\circ}$  à  $3^{\circ}$ , mais en realite, leur technique est differente de celle de GOLDMANN. Ils font remarquer qu'il existe une considerable diminution de l'attention en altitude.

Pour MAC FARLAND, ces resultats contradictoires sont dus aux differences des techniques et surtout d'eclaircissement des tests. Il est bien certain que l'on ne peut guere confronter des experiences menees d'une maniere aussi diverse, mais les erreurs proviennent surtout, selon nous, de la meconnaissance des fluctuations statistiques normales des limites perimetriques. D'experiences faites en perimetrie cinetique sur l'appareil de GOLDMANN modifie, et muni de dispositifs electroniques, nous avons pu conclure que les reponses presentent au sol une dispersion assez considerable. À la peripherie vers  $60^{\circ}$ , leur moyenne est de  $5^{\circ}$ . À la partie centrale, vers  $10^{\circ}$ , elles peuvent atteindre  $10^{\circ}$ .

Nous avons sur 15 sujets repris ces experiences en croisson, avec un perimetre de GOLDMANN, apres mensuration du diametre pupillaire qui ne varie d'ailleurs pas du fait de l'altitude. Le tracé normal des isopteres par la technique habituelle avec plusieurs combinaisons de surface et d'intensite pour le même isoptere, ne nous a montre aucune difference significative entre le sol, les altitudes de 3500, 4000, 6000 et 7000 metres. Nous avons alors recherche systematiquement le lieu de perception d'un test donné presente dans le champ, en allant de la peripherie vers le centre, et nous avons repeté l'experience dix fois pour dessiner le nuage des points obtenus. Au sol la dispersion est de  $5^{\circ}$  dans le meridian oblique vers le superieur avec le test de  $5/1$  à  $50^{\circ}$ , à 4500 metres le nuage de dispersion reste le même. L'inhaltation d' $O_2$  ne modifie rien. Avec un test de  $3/3$  sur le même meridian la dispersion est de  $8^{\circ}$ , entre  $30^{\circ}$  et  $38^{\circ}$ , l'altitude de 4500 metres ou l'inhaltation d' $O_2$  ne changent rien. Il est certain que le fait de ne pas tenir compte de ces dispersions et de leur absence de variation peut faire croire à des differences d'une experience à l'autre. On peut donc conclure que les isopteres restent remarquablement fixes dans les conditions normales d'altitude. Au delà, l'acroembolisme modifie considerablement les choses (Fig 2).

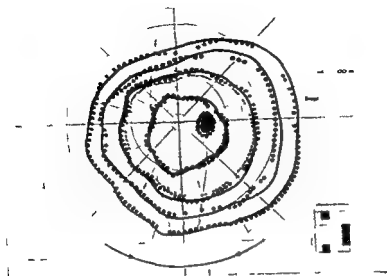


FIG 1

Isoptères du champ visuel à l'altitude de 3200 m — En traits pleins isoptères au sol  
— En pointillé isoptères en altitude

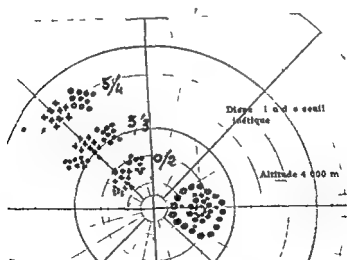


FIG 2

Dispersion de dix réponses avec les tests  $4 \frac{3}{3}$  et  $0 \frac{2}{2}$  Au sol croix — à l'altitude de 4000 m cercles — en altitude sous  $0 \frac{2}{2}$  points noirs. Les nuages de points restent les mêmes en vision périphérique. Par contre autour de la tache de Mariotte ils s'échelonnent concentriquement pour deux tests différents.

FURUYA, sur six sujets, constate à 5000 mètres une contraction débutant du côté temporal, accentuée par la prolongation du séjour en altitude.

LIVINGSTONE avec le périmètre de CARGILL, en utilisant un test de 2 millimètres de diamètre trouve une contraction du champ pour des altitudes de 4500 à 5800 mètres. Elles sont symétriques et suivies parfois d'une tendance à l'élargissement lorsque le séjour en altitude se prolonge. Au-delà de 10000 mètres, apparaissent des modifications plus nettes attribuées à l'aéroembolisme. Nous en reparlerons plus loin.

KARFLEIS et SLIGERT ont repris les expériences de GOLDMANN et SHUBERT avec des tests blancs sur fond gris foncé. Même à des altitudes supérieures à 7000 mètres, ils n'ont pas trouvé de variations dignes d'être retenues. Elles seraient en effet de l'ordre de  $1^{\circ}$  à  $3^{\circ}$ , mais en réalité, leur technique est différente de celle de GOLDMANN. Ils font remarquer qu'il existe une considérable diminution de l'attention en altitude.

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Nous avons sur 15 sujets repris ces expériences en casisson avec un périmètre de GOLDMANN, après mensuration du diamètre pupillaire qui ne varie d'ailleurs pas du fait de l'altitude. Le tracé normal des isoptères par la technique habituelle avec plusieurs combinaisons de surface et d'intensité pour le même isoptère ne nous a montré aucune différence significative entre le sol, les altitudes de 3500, 4000, 6000 et 7000 mètres. Nous avons alors recherché systématiquement le lieu de perception d'un test donné présenté dans le champ, en allant de la périphérie vers le centre, et nous avons répété l'expérience dix fois pour dessiner le nuage des points obtenus. Au sol la dispersion est de  $5^{\circ}$  dans le méridien oblique vers le supérieur avec le test de  $5/4$  à  $50^{\circ}$ , à 4500 mètres le nuage de dispersion reste le même. L'inhérence d'0 ne modifie rien. Avec un test de  $3/3$  sur le même méridien la dispersion est de  $8^{\circ}$  entre  $30^{\circ}$  et  $38^{\circ}$ , l'altitude de 4500 mètres ou l'inhérence d'0 ne changent rien. Il est certain que le fait de ne pas tenir compte de ces dispersions et de leur absence de variation peut faire croire à des différences d'une expérience à l'autre. On peut donc conclure que les isoptères restent remarquablement fixes dans les conditions normales d'altitude. Au-delà, l'aéroembolisme modifie considérablement les choses (Fig. 2).

a depression et nous avons constate que l'elargissement de la tache de Mariotte etait constant en anoxemie et en depression. Elle atteint des proportions importantes et si l'on mesure la tache avec l'index  $3/3$  de Goldman sa surface peut doubler et meme tripler. La grandeur de l'elargissement est une fonction non lineaire de l'altitude et de la vitesse d'ascension (lente dans nos experiences 10 m/sec)

L'elargissement est tres intense de 2000 a 4000 m mais augmente moins au dela. L'inhalation d'oxygene diminue la grandeur de l'elargissement ne ramene jamais la surface de la tache a sa valeur au sol, mais a une valeur intermediaire. Ce fait est a rapprocher de ce que l'on sait du seuil du phenomene.

Nous avons en effet recherche ce seuil. L'elargissement commence des les basses altitudes de 1000 ou 1500 metres, a 2000 m, il est deja tres sensible et semble ne plus progresser que lentement a partir de 4800 metres. A l'altitude de 1500 m l'inhalation d'oxygene reste sans effet sur l'elargissement pourtant deja considerable de la tache. Il semble donc que le phenomene debute par un reflexe baropresseur sans doute auriculaire (Fig 3).

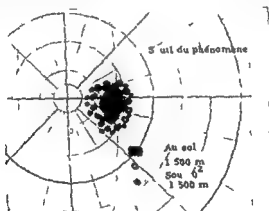


FIG 3

Seuil du phenomene d'elargissement de la tache de Mariotte. Les limites de la tache sont deja plus grandes a 1500 m mais l'action de l'oxygene est peu marquee.

De nombreux facteurs physiologiques sont en cause. Pour les analyser nous avons etudie l'influence de l'altitude sur le skiascotome. Celui-ci a ete produit de deux manieres differentes. La regle d'un double decimetre a ete coincee horizontalement dans l'une des fentes de la coupole de l'appareil de Goldman de maniere a creer un obstacle sur le trajet des rayons du projecteur de tests. Elle portait donc une ombre sur les bords de laquelle apparaissait ou disparaissait le test suivant une loi complexe due a sa forme circulaire. La disparition se produit avec un retard vers l'interieur de l'ombre. L'apparition avec un retard analogue en dehors de l'ombre. Les deux sens d'exploration

Ces expériences ont été néanmoins exécutées pour une seule montée en cuisson d'une minute environ. Les vols très prolongés ne sont pas inoffensifs surtout s'ils sont répétés au dessus du seuil normal d'adaptabilité soit 3,000 m - 3,500 m. HASTFADT a montré sur 20 sujets, les effets cumulatifs de l'anoxiémie en les faisant séjourner 6 jours par semaine, pendant 4 à 6 semaines, 5 à 6 heures par jour à 3000 mètres dans un cuisson. En réalité, les modifications du champ visuel ne purent être démontrées par les procédés classiques en attention concentrée, mais par celui qui consiste à percevoir un test périphérique alors que des couleurs et des formes sont projetées en vision centrale, c'est à dire en attention diffusée. Les modifications persistèrent au sol pendant plusieurs jours et pendant plusieurs semaines chez certains. Il s'agit en réalité beaucoup plus de troubles de l'attention dus à la fatigue, que de modifications proprement dites des seuils dans le champ visuel d'actions corticales que d'actions rétiniennes. On peut donc tenir pour certain que les seuils et leur graphique commode les isoptères, ne varient pratiquement pas pendant le séjour en altitude.

Il n'en est plus ainsi si l'on considère le scotome physiologique situé dans le champ visuel moyen qui constitue la tache de Mariotte. Ses variations sont connues depuis longtemps, GOLDMANN et SHUBERT avaient déjà décrit son élargissement en altitude pour des tests blancs ou colorés. BATENKO et BFIOSTOTSKY, sur 15 sujets, ont fait la même constatation à 5000 mètres. La tache pouvait atteindre jusqu'à 271° de sa superficie normale au sol. L'élargissement disparaissait sous l'influence de l'oxygène.

EVANS et MAC FARLAND travaillant dans une chambre à basse pression d'oxygène, mais sous pression barométrique normale, ont constaté un élargissement des angioscotomes entourant la tache à partir de 4000 mètres. À 5000 mètres, il devient de plus en plus important, créant une oblitération de la partie supérieure du champ visuel et respectant seulement une zone piramculaire de 11 à 10°. L'inhalation d'O<sub>2</sub> assure le retour à la normale.

J. BAILLIART et DUGUET, travaillant sur 8 sujets normaux de 8 à 33 ans, soumis au cuisson à dépression, ne constatent pas de scotome temporel supérieur, mais décrivent par contre, une contraction des limites de la tache, débutant vers 3500 m et croissant jusqu'à 6000 mètres. Cette contraction est de l'ordre de 6 à 80°, avec une moyenne de 38°. Après retour au sol la récupération est normale mais chez certains sujets, la tache s'élargit. L'inhalation d'oxygène en altitude corrige la contraction anoxémique. Par contre l'inhalation d'oxygène pris à 100° élargit la tache.

ROSENTHAL n'est cependant pas de cet avis et soutient que l'inhalation d'oxygène pris au sol provoque la contraction de l'angioscotome. La strychnine en inhalations donnerait aussi au sol une réduction considérable de la surface du scotome et corrigerait dans une certaine mesure l'élargissement anoxémique.

Les auteurs ne sont donc pas d'accord. Nous avons repris ces expériences avec le périmètre de Goldmann monté dans un cuisson

## GENERAL CONCEPTS OF EALES'S DISEASE

By LALIT P AGARWAL,

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Eales's (1880)<sup>(1)</sup> described the clinical syndrome of periphlebitis associated with recurrent vitreous haemorrhage in young individuals. The syndrome is characterised by the presence of perivascular exudates with massive haemorrhages along one or more of the retinal veins and into the vitreous. Haemorrhages in the vitreous ultimately result in the formation of glial bands projecting into the vitreous and ending into a traction detachment of retina.

The aetiology of the disease is unknown and more often than not it is considered to be tubercular<sup>(2-6)</sup> or tuberculo allergic in origin.<sup>(9, 14)</sup>

We investigated a series of 50 cases of Eales's disease for Mantoux's reaction. Our results reveal that only 16 of the 50 cases show tuberculin sensitivity in titres of 1/10,000 or over and in only 2 cases this reaction was positive in a titre of 1/100,000. The results are in no way different from a similar number of normal cases (Table 1).

Recent reports of fundus changes in sickle cell disease and abnormal haemoglobin conditions have focussed our attention to this aspect of pathogenesis of the disease.<sup>(14, 19)</sup>

Our cases were studied for the presence of any evidence of sickling red blood cells or abnormal haemoglobin. We employed the technique of depriving the RBC of oxygen for the detection of the presence of sickle cells. Electrophoretic method with veranol solution as buffer at PH 8.6 was used for determining the abnormal haemoglobins. The electrophoretic pattern of the haemoglobin of our cases did not differ from the haemoglobin of normal individuals. The lack of sickling of RBC and the normal electrophoretic patterns, of haemoglobin (Figs 1 to 4) in cases of Eales's disease allows us to conclude that though vitreal and retinal haemorrhages are seen in sickle cell disease yet the two diseases are unrelated and sicklaemia has no aetiological bearing on Eales's disease.

We also investigated the cases of this series for any evidence of macroglobulinaemia by the electrophoretic method and dilution plasma method but no evidence of macroglobulinaemia was found (Fig 5).



a depression et nous avons constate que l'elargissement de la tache de Mariotte etait constant en anoxemie et en depression. Elle atteint des proportions importantes et si l'on mesure la tache avec l'index 3/3 de Goldmann sa surface peut doubler et meme tripler. La grandeur de l'elargissement est une fonction non lineaire de l'altitude et de la vite de l'ascension (lente dans nos experiences 10 m/sec).

L'elargissement est tres intense de 2000 a 4000 m mais augmente moins au dela. L'inhalation d'oxygene diminue la grandeur de l'elargissement, ne ramene jamais la surface de la tache a sa valeur au sol mais a une valeur intermediaire. Ce fait est a rapprocher de ce que l'on sait du seuil du phenomene.

Nous avons en effet recherche ce seuil. L'elargissement commence des les basses altitudes de 1000 ou 1500 metres, a 2000 m il est deja tres sensible et semble ne plus progresser que lentement a partir de 4800 metres. A l'altitude de 1500 m, l'inhalation d'oxygene reste sans effet sur l'elargissement pourtant deja considerable de la tache. Il semble donc que le phenomene debute par un reflexe baropresseur sans doute auriculaire (Fig 3).

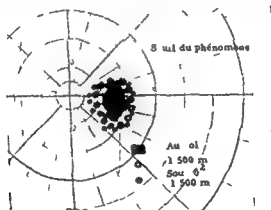


FIG 3

Seuil du phénomène d'élargissement de la tache de Mariotte. Les limites de la tache sont déjà plus grandes à 1500 m mais l'action de l'oxygène est peu marquée.

De nombreux facteurs physiologiques sont en cause. Pour les analyser nous avons étudié l'influence de l'altitude sur le skiascotome. Celui-ci a été produit de deux manières différentes. La règle d'un double décimètre a été coincee horizontalement dans l'une des fentes de la coupole de l'appareil de Goldmann de manière à créer un obstacle sur le trajet des rayons du projecteur de tests. Elle portait donc une ombre sur les bords de laquelle apparaissait ou disparaissait le test suivant une loi complexe due à sa forme circulaire. La disparition se produisait avec un retard vers l'intérieur de l'ombre, l'apparition avec un retard analogue en dehors de l'ombre. Les deux sens d'exploration

Ces expériences ont été néanmoins exécutées pour une seule montée en caisson d'une matinee environ. Les vols très prolongés ne sont pas inoffensifs surtout s'ils sont répétés au dessus du seuil normal d'adaptabilité soit 3,000 m - 3,500 m. HALSTEADT a montré sur 20 sujets, les effets cumulatifs de l'anoxémie en les faisant séjourner 6 jours par semaine, pendant 4 à 6 semaines, 5 à 6 heures par jour à 3000 mètres dans un caisson. En réalité, les modifications du champ visuel ne purent être démontrées par les procédés classiques en attention concentrée, mais par celui qui consiste à percevoir un test périphérique alors que des couleurs et des formes sont projetées en vision centrale, c'est-à-dire en attention diffusée. Les modifications persistèrent au sol pendant plusieurs jours et pendant plusieurs semaines chez certains. Il s'agit en réalité beaucoup plus de troubles de l'attention dus à la fatigue, que de modifications proprement dites des seuils dans le champ visuel d'actions corticales que d'actions rétiniennes. On peut donc tenir pour certain que les seuils et leur graphique commode les isoptères, ne varient pratiquement pas pendant le séjour en altitude.

Il n'en est plus ainsi si l'on considère le scotome physiologique situé dans le champ visuel moyen que constitue la tache de Mariotte. Ses variations sont connues depuis longtemps, GOLDMANN et SHUBERT avaient déjà décrit son élargissement en altitude pour des tests blancs ou colorés. BATENKO et BELOSTOTSKY, sur 15 sujets, ont fait la même constatation à 5000 mètres. La tache pouvait atteindre jusqu'à 271% de sa superficie normale au sol. L'élargissement disparaissait sous l'influence de l'oxygène.

EVANS et MAC FARLAND travaillant dans une chambre à basse pression d'oxygène, mais sous pression barométrique normale, ont constaté un élargissement des angioscotomes entourant la tache à partir de 4000 mètres. À 5000 mètres, il devient de plus en plus important, créant une oblitération de la partie supérieure du champ visuel et respectant seulement une zone perimaculaire de 8 à 10°. L'inhalation d' $O_2$  assure le retour à la normale.

J. BAILLIART et DUGUET, travaillant sur 8 sujets normaux de 18 à 33 ans, soumis au caisson à dépression, ne constatent pas de scotome temporal supérieur, mais décrivent par contre, une contraction des limites de la tache, débutant vers 3500 m et croissant jusqu'à 6000 mètres. Cette contraction est de l'ordre de 6 à 80%, avec une moyenne de 38%. Après retour au sol, la récupération est normale mais chez certains sujets, la tache s'élargit. L'inhalation d'oxygène en altitude corrige la contraction anoxémique. Par contre, l'inhalation d'oxygène pris à 100% élargit la tache.

ROSENTHAL n'est cependant pas de cet avis et soutient que l'inhalation d'oxygène pris au sol provoque la contraction de l'angioscotome. La strychnine en injections donnerait aussi au sol une réduction considérable de la surface du scotome et corrigerait dans une certaine mesure l'élargissement anoxémique.

Les auteurs ne sont donc pas d'accord. Nous avons repris ces expériences avec le périmètre de Goldmann monté dans un caisson

Une deuxième série d'expériences a été faite avec deux lames de polaroid orientées à 90 l'une de l'autre. L'une était suspendue dans la coupole sur le trajet des rayons du projecteur, l'autre était montée sur l'objectif de projection lui-même. Lorsque les rayons polarisés du projecteur rencontraient le disque de polaroid suspendu la lumière s'éteignait. On obtenait ainsi un skiascotome plus maniable que le précédent car la variation des axes de polarisation permettait de ne pas supprimer complètement la lumière et de lui donner seulement des valeurs infra-luminaires pendant la traversée du skiascotome. Les expériences ont été faites à 15° sur le méridien nasal horizontal. L'altitude et l'oxygène n'ont eu aucune influence (Fig. 6).

Ces constatations permettent une interprétation. Le skiascotome qui crée une ombre artificielle et de dimensions fixes sur la rétine, ne varie pas. L'angioscotome tributaire des vaisseaux varie. Le phénomène est donc vraisemblablement dû à la circulation rétinienne. La fixation des isoptères et du skiascotome exprime par contre les propriétés de résistance du tissu nerveux lui-même aux conséquences de la pression et de l'anoxémie. D'autre part, le seuil incroyablement bas du phénomène d'élargissement de la tache de Mariotte, le peu d'effet de l'oxygène à ces basses altitudes permet de penser que l'explication ne réside pas uniquement dans l'anoxémie. Un réflexe baropresseur auriculo-oculaire doit aussi être en cause. On sait en effet les rapports de la physiologie auriculaire avec celle de l'angioscotome.

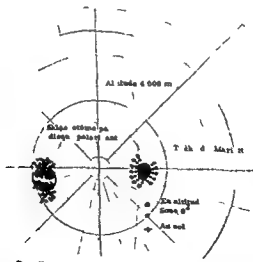


FIG. 6

Skiascotome analysé par un système de polarisation. Les points obtenus en pénétrant dans l'ombre ou en en sortant sont mélangés qu'ils correspondent au sol à l'altitude de 4000 m ou à l'inhalation d'oxygène. Autour de la tache de Mariotte ils s'étagent concentriquement.

ont été captables. Nous n'avons constaté aucune modification en altitude ou par inhalation d'oxygène (figs 1 et 5).



Fig. 4

Skizze eines Typus für ein Gebäude mit typischer Ausrichtung in der Höhe. Die Punkte sind die Höhenpunkte der Gebäude und der Umgebung.



Fig. 5

Skizze eines Typus für ein Gebäude mit typischer Ausrichtung in der Höhe. Die Punkte sind die Höhenpunkte der Gebäude und der Umgebung. Die Punkte sind die Höhenpunkte der Gebäude und der Umgebung. Die Punkte sind die Höhenpunkte der Gebäude und der Umgebung.

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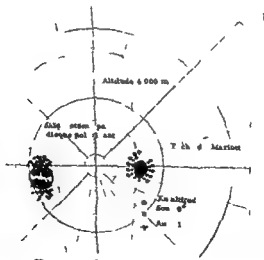


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ont été employés. Nous n'avons constaté aucune modification en altitude ou par inhalation d'oxygène (Figs 4 et 5)

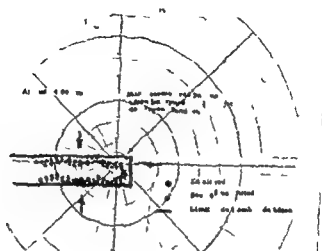


FIG 4

Skiascotome créé par un bâton interposé sur le trajet des rayons lumineux du projecteur périmétrique à l'altitude de 1000 m

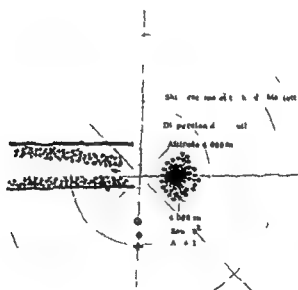


FIG 5

Skiascotome au sol, à 1000 m et sous  $O_2$  à 4000 m. Les points représentant les endroits où le test pénétrant dans l'ombre du bâton cesse d'être perçue sont mélangés au sol à 1000 m et sous oxygène. Autour de la tache de Mariotte, ils s'étagent au contraire concentriquement. Les plus externes correspondent à l'altitude de 4000 m, les moyens sont obtenus à la même altitude sous  $O_2$ .

peripheriques se retrecissent. Mais ces phenomenes sont tres individuels et l'on peut classer les sujets en tolerants et intolerants a l'altitude. L'anoxemie fait apparaitre dans le champ des flocons nuageux gris rougeatres qui se deplacent en vagues successives du centre vers la peripherie. Les nuages deviennent de plus en plus apparents au fur et a mesure que l'anoxemie s'accroît. L'inhalation d'oxygene fait apparaitre une lueur bleue intense, parfois verdâtre au niveau du point de fixation. Le deplacement des nuages devient plus rapide puis ils disparaissent et les objets peuvent a nouveau etre identifiés. Les seuils absolus paraissent plus eleves en anoxemie quoique les processus d'adaptation ne soient pas troubles d'après LIVINGSTONE. Nous n'avons pas d'experience personnelle sur ce sujet.

## II ACCELERATIONS—

Les modifications de la pression et de l'oxygenation ne sont pas les seuls facteurs de perturbation du champ visuel au cours du vol. Les accelerations ou les decelerations entraînent des variations considerables qui peuvent aller jusqu'à la perte totale de la vision. Les accelerations angulaires etaient redoutées en aviation classique surtout lors des piques, mais les rectilignes prennent une grande importance du fait de l'emploi des fusées destinées a echapper à l'attraction terrestre (Stewart Franks, Herr et Rose, Ruff et Strughold, Marshall, Diringshofen, Andrina). Un voile gris apparait en general pour des accelerations tête siege a partir de 4G. Si le pilote maintient cette valeur d'acceleration trop longtemps ou voisine 5G le voile noir apparait rapidement. Il debute du côté nasal et masque bientôt tout le champ visuel. Un degre de plus et le pilote perd conscience. Peu de documents precis ont été donnes sur ce phenomene. Des lampes colorees ont été placees dans le champ visuel du pilote. La disparition des lampes peripheriques l'avertit de la perte du champ surtout nasal et commande de desserrer le virage. Les temps necessaires a la perte de la perception des lampes successives suivant les accelerations sont les seules donnees connues actuellement, la morphologie des champs n'ayant pas été étudiée a notre connaissance ou n'ayant pas fait l'objet de publications. Le voile noir est attribue a la fuite du sang vers les territoires veineux des membres inferieurs creant une anemie cerebrale. L'ischemie retinienne serait aidée par la pression oculaire d'après Diringshofen et d'après Andrina, d'où l'apparition du voile noir avant la perte de conscience. Mais l'ischemie carotidienne doit diminuer cette pression, facteur dont on n'a pas tenu compte les auteurs. Oh je pose aussi la question de savoir pourquoi dans ces conditions la compression oculaire permettrait une resistance accrue aux accelerations? Seule la connaissance des champs visuels permettra de trancher le debat et de savoir si l'origine du phenomene est cerebrale ou retinienne.

Les accelerations tête siege sont plus rares. Elles elevent la pression dans les vaisseaux cerebro-retiniens a — 2 G. elles creent avec la céphalée des scotomes negatifs dont la forme, la surface et la position sont mal connues. Elles donnent surtout lieu au voile rouge.

Ces conclusions sont en désaccord partiel avec des expériences faites par Bietti. Cet auteur a constaté que l'inhalation d'oxygène retrecit les angioscotomes normaux et ceux de plusieurs maladies, surtout du glaucome. Cependant, dans 20% des cas, l'angioscotome pourrait s'élargir, ce qui expliquerait les effets constatés par DUGUET et J. P. BAILLIART, complètement opposés à ceux de ROSENTHAL. Le skiascotome, pour BIELTI, retrecirait par contre constamment sous l'influence de l'oxygène, ce qui indiquerait une amélioration de la fonction rétinienne, se traduisant par une disparition plus lente et une apparition plus rapide du test. Le résultat sur l'angioscotome de l'oxygène ou de sa privation serait expliqué par le jeu des facteurs qui agissent sur son étendue : calibre vasculaire, grandeur du flux sanguin, sensibilité rétinienne. En général, la privation d'oxygène diminue la sensibilité rétinienne en même temps qu'elle crée la vasodilatation. L'angioscotome et la tache de Mariotte s'élargissent, ce qui est en accord avec les données de la majorité des auteurs. Mais chez certains sujets, le calibre des vaisseaux diminue et l'angioscotome serait plus étroit malgré la diminution de la sensibilité rétinienne.

Les modifications de calibre des vaisseaux pourraient donc être variables suivant les sujets, mais le skiascotome varierait toujours dans le même sens et serait ainsi plus fidèle que l'angioscotome. Nous n'avons pas retrouvé cette variation du skiascotome. La aussi, la dispersion statistique des réponses est considérable au niveau de ses bords, et il est nécessaire d'en tenir compte, conformément à ce que nous avons dit plus haut pour la mesure des isoptères.

Il résulte néanmoins des études des auteurs et de nos propres expériences que dans les effets de l'anoxémie et de la dépression, se mêlent les modifications vasculaires rétiniennes et les troubles de la sensibilité du tissu nerveux proprement dit.

Ce qui précède concerne les dépressions relativement lentes de l'ordre de 10 m sec. Les décompressions brusques sont différentes dans leurs effets. Elles provoquent l'apparition d'altérations du champ visuel périphérique avec contractions irrégulières du champ que la montée lente vers l'altitude ne peut produire. D'après WHITTER, il y aurait aussi des scotomes bilatéraux et homonymes se déplaçant par un mouvement centrifuge vers la périphérie du champ visuel. Ils s'effacent rapidement en 10 à 16 minutes après le retour au sol. La région maculaire n'est jamais intéressée et les dimensions de la tache aveugle ne seraient pas modifiées. LIVINGSTONE constate aussi des scotomes multiples avec contraction périphérique des champs. Ces manifestations coïncident souvent avec un syndrome migraineux classique, accompagné de céphalées et de tendances syncopales. On les interprète souvent comme des conséquences de l'acroembolisme dans les artérioles terminales et de spasmes surajoutés.

Le champ visuel nocturne présente des modifications assez différentes de celles du champ photopique. D'après LIVINGSTONE, le scotome maculaire nocturne normal s'élargit en même temps que la tache de Mariotte, qui réagit comme en vision diurne. Les limites



produit pas dans la lecture des appareils de bord, l'éblouissement est donc surtout périphérique et gêne alors la vision centrale.

Il s'apparente de loin et tout au moins en ce qui concerne l'ambiance générale, à ce qui se produit lorsqu'au laboratoire un sujet est soumis à une luminance de préadaptation puis plonge dans l'obscurité. Dans l'aéronef, la deuxième ambiance reste lumineuse, mais il existe un passage où les sens sont très fortement perturbés dans leur valeur et leur topographie et par conséquent inadéquats. Nous ne connaissons pas de travaux précis sur cette question de l'éblouissement général. Le sujet restant en lumière photopique ou mésopique les recherches actuelles portant surtout sur l'éblouissement de la région centrale du champ visuel.

De nombreuses recherches restent à faire sur le comportement du champ visuel en haute altitude et tout est loin d'être dit sur ce sujet. Les premières acquisitions sont cependant d'un haut intérêt, à la fois pratique et théorique et suscitent des interprétations physiologiques difficiles.

L'expérimentation a été faite au centre physiologique de l'armée de l'Air Française qui a mis généreusement à notre disposition ses caissons à dépression. Nous remercions tout particulièrement le Médecin Commandant Perdriel de l'amabilité avec laquelle il s'est constamment tenu à notre disposition.

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dont l'interprétation est encore plus difficile que celle du voile noir. En effet, la repletion excessive des vaisseaux rétiniens en pathologie ne donne pas la sensation de rouge.

On sait que des études très poussées ont été faites, grâce à des machines centrifugeuses pour tenter d'éviter les phénomènes de voile noir et de voile rouge et d'augmenter la résistance aux accélérations. La position couchée diminue le gradient de pesanteur tête-tronc, on résiste donc mieux dans cette position aux accélérations. Mais deux positions sont possibles, l'accélération se produisant dans le sens face antérieure, face postérieure du thorax, ou "eyeballs in" comme disent les auteurs anglais, ou dans le sens face postérieure, face antérieure "eyeballs out". Cette dernière position serait la meilleure, mais provoquerait un flot de larmes très gênant pour le pilote. Les positions couchées, sur le côté sont préjudiciables au fonctionnement cardiaque.

On admet en général qu'un pilote en position ordinaire sur son siège sans protection spéciale, peut supporter 5 G d'accélération et — 3 G dans l'autre sens, une combinaison élastique réduisant les déplacements sanguins augmente la tolérance à 6 G. La tolérance aux accélérations en ligne droite, qui est le cas des fusées, serait plus forte, 8 G avec eyeballs in, et plus de 8 G avec eyeballs out. Mais le flot de larmes se produit comme nous venons de le dire. On envisagerait même d'immerger entièrement le corps du pilote dans une cuve remplie d'eau. L'accroissement d'inertie du corps serait alors contrebalancé par l'inertie de l'eau. La tolérance pourrait monter à 32 G, pendant 5 secondes.

Les conséquences de l'état d'apesanteur sur l'œil sont mal connues. Les équipes soviétiques n'ont rien rapporté sur ce sujet. La centrifugeuse est ici inutilisable et seul un parcours parabolique rigoureusement contrôlé en avion peut produire cet état pendant une fraction très courte de temps. Il semble que rien ne se produise du point de vue visuel, mais on ne sait pas si la prolongation de cette situation ne pourrait pas retentir sur l'œil par un mécanisme indirect de modifications hydriques vasculaires et de régulation nerveuse.

Quoiqu'il en soit, l'étude des phénomènes oculaires dus à l'accélération et surtout porte sur leurs conditions d'apparition plus que sur l'analyse méthodique de leurs modalités et de leur mécanisme intime.

### III EBLouisSEMENT

Restent enfin les phénomènes d'éblouissement qui proviennent de la modification de l'ambiance lumineuse et qui peuvent perturber grandement le champ visuel. Le ciel est assombri en haute altitude mais les objets éclairés par les rayons solaires deviennent très brillants. Les nuages, les plans métalliques réfléchissent violemment la lumière. Les postimages sont très intenses, persistant longtemps de 2 à 3 minutes. Toutes les variétés d'éblouissement peuvent se voir, périphérique ou central. Celui-ci n'est pas le plus fréquent puisque le pilotage à ces altitudes n'est plus une question de visibilité extérieure. Il ne se

### AETIOLOGY

Being unable to find any evidence of other disease to account for the hæmorrhage he was inclined to attribute the syndrome to a disturbance of autonomic control "affecting both the circulatory organs and the digestive system leading on the one hand to partial inhibition of the muscular movements of the bowels and to vaso motor contraction of the vessels of the alimentary canal with inhibition of its secretory functions and on the other hand to compensatory dilatation of the systemic capillaries especially those of the head, and in these cases of the retina causing over distention of the venous system with liability to rupture on the occurrence of any intensifying cause." He considered this an explanation of the headache, epistaxis, retinal hæmorrhages and the tortuosity and fullness of the retinal vessels and temporal artery.

### TREATMENT

Having tried various remedies he concluded that there was no evidence of their doing much good and contented himself with symptomatic treatment. It will be interesting to learn what progress has been gained in our knowledge of the aetiology and treatment of this condition in the 80 years since the time of Eales's description and if any further information has been obtained on the part played, if any, by the autonomic nervous system in this condition.

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# ASPECTS CLINIQUES DE L'ANOXIE EN OPHTALMOLOGIE AERONAUTIQUE

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Malgré les progrès réalisés par l'Aéronautique moderne, et l'emploi de moyens permettant de maintenir un apport suffisant d'oxygène aux sujets se trouvant même aux altitudes les plus élevées le problème de l'anoxie reste actuel en médecine aéronautique et spatiale

Parmi les manifestations de l'anoxie, celles relatives à l'organe visuel occupent une place importante. Depuis de nombreuses années elles ont intéressé mes collaborateurs et moi-même et je me rapporterai principalement à nos études au cours de cet exposé.

Nous pouvons étudier les modifications provoquées par l'anoxie avec avant tout les moyens utilisés dans la physiologie aéronautique, qui permettent de reproduire à terre les conditions d'hypoxie. Nous voulons parler de l'emploi des chambres à dépression de l'inhalation de mélanges gazeux pauvres en oxygène et de la méthode de rérespiration.

Des résultats superposables peuvent être obtenus en ce qui concerne l'exploration de certaines fonctions oculaires par la compression dynamométrique du globe oculaire qui entraîne une ischémie locale. Cela permet de mettre en évidence que l'action du déficit en oxygène sur certaines fonctions (sens lumineux, acuité visuelle centrale et périphérique, dimensions des scotomes physiologiques, sens chromatique, fréquence critique de fusion, etc.) est en grande partie expliquée par des phénomènes au niveau de la rétine.

L'anoxie entraîne au niveau de l'appareil visuel des altérations de type *sensitivo sensoriel*, des *altérations circulatoires*, des *troubles de la motilité oculaire intrinsèque et extrinsèque* et enfin des *modifications de la transparence des milieux oculaires*.

En ce qui concerne les *modifications sensitivo sensorielles*, je rappellerai que le déficit en oxygène a seulement une action modeste sur l'*acuité visuelle centrale* <sup>2, 47-52</sup> sauf en vision à basse illumination où la diminution de l'acuité visuelle est plus nette <sup>33</sup> elle a une action similaire sur le *pouvoir de résolution* de la rétine <sup>14</sup>. Les phénomènes sont évidents seulement à haute altitude.

Les *limites périphériques du champ visuel* ne sont que peu modifiées <sup>20-24-26, 57</sup> mais on signale parfois des scotomes. Les scotomes

physiologiques rencontrés chez les sujets normaux subissent des modifications plus importantes. On observe en général un élargissement de la tache veugle (3-22-7) sous effet de l'anoxie, accompagnée par un élargissement des angioscotomes (50-51-7) qui en partent. Dans un certain nombre de cas, au contraire, on observe un phénomène opposé, c'est à dire leur diminution (40-7). Il faut interpréter ces différences comme étant en rapport avec un comportement différent du calibre vasculaire selon les sujets. L'exploration de la sensibilité rétinienne par un moyen plus précis, c'est à dire la détermination du scotome artificiel de Goldmann ou "sclascotome" par la méthode de la "riche d'huile", met en évidence une augmentation constante de ce scotome sous l'effet de l'anoxie, (7) cela révèle une diminution de la sensibilité rétinienne.

L'acuité visuelle stéréoscopique est peu influencée par l'anoxie à altitudes moyennes, alors qu'il y a accentuation des troubles à des altitudes supérieures (16) (6-8,000 m). La dimension des images rétiniennes (isotomie) (44) n'est pas modifiée par le déficit en oxygène.

Les sens lumineux (21-23-29-33-34-35-36-37) est très sensible à l'anoxie. Ces altérations se relevent déjà à des altitudes moyennes (2 500 m) et augmentent avec l'altitude. On a interprété ce phénomène de différentes façons, (43) en l'attribuant à des modifications du métabolisme des substances photochimiques rétiniennes, et de la position du pigment rétinien, à des troubles de la circulation, mais surtout à une action directe sur les éléments nerveux, qui se sont relevés comme ayant particulièrement besoin d'oxygène et l'obscurité.

Le sens chromatique n'est pas fortement influencé par le déficit en oxygène, mais si l'on emploie des techniques d'examen précises, il y est toutefois sensible. L'anomaloscope permet ainsi de constater l'apparition de légères protanomalies ou deuteranomalies, (17) ainsi que l'augmentation de l'amplitude de déplacement de la vis, lors de la détermination de l'équation de Rayleigh. On constate une aggravation des troubles chez les sujets ayant déjà un sens chromatique défectueux. Le test de Farnsworth indique également des anomalies, et en particulier l'apparition d'une tritanomalie (18). L'anoxie entraîne, de plus, lorsqu'elle est élevée, des altérations de la efficacité chromatique dans le bleu, dans le vert et dans le jaune au "color aptitude test" (52).

L'anoxie a de plus la caractéristique de réduire la fréquence critique de fusion (10) des stimulus lumineux répétés, surtout au niveau de la partie centrale de la rétine, mais aussi, lorsque l'anoxie est élevée, de la portion périphérique. L'ischémie du globe oculaire entraîne des résultats analogues.

L'examen en anoxie des deux indices d'excitabilité rétinienne et plus précisément de la *theobase* et de la *chronaxie optiques*, a mis en évidence une diminution de l'excitabilité de ces deux indices déjà à des altitudes peu importantes (2 000 m), en particulier en ce qui concerne la *chronaxie* (50).

L'activité électrique de la rétine (*electroretinogramme*) est aussi altérée par le déficit en oxygène. La composante négative de l'ERG (onde a) serait, selon certains auteurs (15) plus résistante à l'anoxie que l'onde positive b et l'onde x ceci surtout chez le chat mais aussi chez l'homme (19) lorsque l'anoxie est élevée. Nous avons au contraire personnellement trouvé une diminution de l'onde a sans changements du trace (1).

D'autres observations traduisent les variations du comportement du réflexe oculo-cardiaque (48) (augmentation du seuil avec sensibilité moindre lors du déficit en oxygène) et de la sensibilité cornéenne (augmentée dans l'anoxie aussi bien aiguë (32) que chronique) (57). L'anoxie influe de plus sur les phénomènes de *révolite rétinienne*, (46) augmentant de façon toutefois légère, l'inhibition.

Rappelons enfin, l'influence sur les *phénomènes endoptiques* se révélant par l'apparition spontanée de phosphènes et la diminution de la visibilité des houppes de Hardinger. Le comportement des images posthumes (25-39) est intéressant il y a une augmentation de la période de latence qui est inversement proportionnelle à l'importance du stimulus qui entraîne leur apparition, et une prolongation de leur durée cela explique certains phénomènes d'éblouissement constatés aux hautes altitudes par ex lors du vol au dessus des couches compactes des nuages reflétant fortement la lumière (55).

Quant aux *altérations circulatoires* (40) dues à l'anoxie notons avant tout l'augmentation de la pression artérielle rétinienne (11) dans la majorité des cas (75%) avec accélération de la circulation rétinienne, diminution du calibre vasculaire, augmentation du tonus des vaisseaux coloration violacée des artères à l'ophtalmoscope. Dans l'anoxie chronique des altérations plus graves de la rétine apparaissent hémorragies et œdèmes (54).

La *pression oculaire* est aussi influencée, mais de façon légère. On observe une faible élévation lors de l'anoxie aiguë (11) et dans la décompression et une faible diminution dans celle chronique (30). La *perméabilité de la barrière hémato-ophthalmique* est augmentée (28-29a, 29b).

L'anoxie entraîne des modifications importantes au niveau de la *musculature oculaire intrinsèque et extrinsèque*.

On observe l'apparition d'une légère exophtalmie (56) par hyperexcitabilité sympathique lors de l'anoxie chronique avec de plus des altérations de la *mobilité pupillaire* (13) et de l'*accommodation*, ainsi que de la musculature extrinsèque du globe oculaire.

Les pupilles en effet se dilatent et le miosis provoque par l'illumination est plus bref et moins prononcé. Cependant la vitesse de contraction et de décontraction pupillaire augmente. L'effet de restitution obtenu par les stimuli acoustiques sur la pupille est moindre ou même absent quand l'anoxie est grave et le stimulus lumineux faible la pupille peut même devenir tout à fait inexcitable. Signalons un phénomène singulier l'apparition d'anisocorie statique



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gueries déclanchement ou aggravation d'un nystagmus latent L'administration d'oxygène inhale à la pression atmosphérique exerce au contraire une action opposée, qu'on peut utiliser dans des buts thérapeutiques, même si ses effets sont transitoires

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ou dynamique, ou bien la disparition d'inégalités pré existantes lors du déficit en oxygène

En ce qui concerne l'accommodation, on note chez les presbyopes, au début un éloignement majeur du *punctum proximum*, mais aussi, chez les sujets jeunes, une augmentation du temps d'accommodation et de la fatigue accommodative. Ce phénomène est beaucoup plus accentué dans la vision binoculaire que dans celle monoculaire, en raison évidemment, de la plus grande sensibilité des muscles striés de la convergence, les muscles lisses du corps ciliaire étant moins sensibles. En effet, la convergence est facilement fatigable dans l'anovie alors que le *punctum remotum* de la convergence s'éloigne.

On observe encore d'autres troubles de la musculature oculaire (8) lors de l'anovie, en général on constate une tendance à l'exophorie dans la vision éloignée (qui peut requière une exophorie pré existante), une tendance au contraire pour l'exophorie dans la vision de près, et aussi l'apparition de déséquilibres verticaux, et, exceptionnellement, de diplopie. L'alcool (8) potentialise les effets de l'anovie, même modestes. Le pouvoir de fusion (9) est réduit en anovie, surtout en réduction, l'amplitude de fusion est au contraire mieux conservée, si l'anovie n'est pas très grave.

Elle détermine aussi des troubles des mouvements oculaires associés, comme par ex. ceux de la lecture (12). On constate une augmentation du temps employé pour lire un texte, un ralentissement des mouvements oculaires, une augmentation des erreurs avec mouvements de retour, une augmentation du nombre des fixations des groupes de lettres, une plus grande fréquence du clignement.

Dans le groupe des alterations de la motilité oculaire, signalons enfin les modifications provoquées par l'anovie sur le nystagmus optocinétique, (47) dont la fréquence est réduite alors que l'on observe une légère augmentation de l'amplitude des secousses.

Je rappellerai enfin que l'anovie provoque d'étranges alterations de transparence des milieux oculaires. En dehors des troubles superficiels transitoires de la cornée, provoqués par l'emploi prolongé des verres de contact (qui entraînent une sorte d'isphymie), ou par le séjour dans une atmosphère d'azote, nous signalons surtout les opacifications du cristallin, que l'anovie grave et l'isphymie provoquent chez le rat (4, 5, 41, 42) et, de façon moindre, chez le lapin (41, 42) mais non chez l'homme, elles sont réversibles. Ces opacités peuvent être expliquées par une diminution de la pression osmotique de l'humeur aqueuse, une chute des chlorures, une augmentation de la production d'acide lactique.

En dehors des modifications que j'ai énumérées jusqu'ici et qui sont déterminées par l'anovie chez les sujets ayant un appareil oculaire normal, je pense qu'il est intéressant de rappeler que lorsqu'il y a des alterations oculaires, (6) celles-ci peuvent être aggravées par un déficit en oxygène : élargissement de scotomes de différentes origines (y compris ceux observés dans le strabisme en vision monoculaire et binoculaire), réapparition d'une diplopie lors de crises apparemment

## SPACE OPHTHALMOLOGY

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Aerospace ophthalmology is a continuing extension of aviation ophthalmology, a discipline that was created when aviation medicine developed into a well organized science during the early years of the twentieth century. It is highly dependent upon the teachings and experience gained from clinical ophthalmology but possesses a number of distinct and unique features that set it apart.

Historically the ophthalmologist has occupied a primary role in aviation medicine. The acknowledged father of aviation medicine in America was an ophthalmologist, General Theodore C. Lyster (2).

The first Aviation Medical Research Laboratory in the United States was established at Hazelhurst Field, in Mineola, Long Island, in 1918. Its director was an ophthalmologist, Colonel William H. Wilmer, and the Chief of the Ophthalmology Department was Dr. Conrad Berens. Outstanding basic work performed at this laboratory developed many of our present concepts. Studies dealing principally with the effects of oxygen lack upon visual acuity, accommodation, convergence, and retinal sensitivity led Drs. Berens and Wilmer to conclude that the visual symptoms taking place during decompression, or at altitude, were due to lack of oxygen and not to the reduction of barometric pressure as had been claimed by some authors (19).

A perusal of aviation medicine literature discloses many other well known contributors in the field of ophthalmology that I am unable to credit at more length in this paper. Many of the problems that we now face in aerospace flight are not entirely new, and the research performed by early workers has contributed significantly to our present successes in space flight.

Since man's creation, he has reached out to conquer new frontiers with unshakable faith and has turned his dreams into reality. Throughout the ages man has felt the compelling attraction of the stars and planets, longing for the day when he might experience the fascination of flight into space. This era was ushered in with startling abruptness on October 4, 1957, when the Soviet Union orbited the unmanned artificial earth satellite, *Sputnik I*. Within a few months this was followed by *Sputnik II*, containing the first space dog, and then by the United States satellite *Explorer I*. These rapidly occurring successes in space exploration made the peoples of the world suddenly realize that the age of manned space flight was rapidly approaching.

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Eales's disease has also been ascribed to the hormonal disorders like hypopituitarism<sup>(20, 21)</sup> and relative deficiency of androgens. We have not done any hormonal assays but therapy with androgens has given equivocal results suggesting indirectly that deficiency of androgens is probably not a causative factor.

Deficient oxygen carrying capacity of the blood may affect the capillary walls of the retinal blood vessels leading to retinal and vitreal haemorrhages. We estimated the oxygen concentration by Van Slyke's method in 50 normal individuals and 50 cases of Eales's disease of the same age group. Our observations do reveal that in a majority of cases of Eales's disease the oxygen concentration of the blood was subnormal (Table II). This deficiency probably leads to venospasms, oedema or retinal increase in fragility of small capillaries and greater permeability of venules and exudation.

The aetiology of Eales's disease is as yet uncertain and remains conjectural. Deficient oxygen carrying capacity without sickling of R.B.C. is an important finding and the factors producing this deficiency of oxygenation require further experimentation.

#### CLINICAL PICTURE

The disease is conventionally described to be present in apparently healthy young males. In this series only two cases were seen in females and the rest were males. The minimum age in this series was 18 years and the maximum age was 45 years. Those in the later age group came in 4th or 5th attack. The average age of the onset of the disease has been 23 years.

Eales had pointed out that in most of the cases the L.L. is affected earlier than the right eye and this observation is fully supported by our series as in 32 of the 50 cases either the left eye was the only involved eye or it was affected earlier than the right eye.

The patient complains of a sudden painless blurring of vision on awakening in the morning. The degree of blurring depends on the extent of haemorrhage and the vision may even be reduced to perception of light. One eye is involved earlier than the other but eventually both eyes are affected. The ophthalmoscopic picture depends upon the severity of the haemorrhage. If there is massive haemorrhage in the vitreous fundus reflex is absent but a black or faint red reflex may be seen. If the haemorrhage is minute and the patient complains of only few black spots in the visual field the vitreous may look clear and haemorrhages can be seen in the retina. Intermediate grades of haemorrhages in the vitreous may be visible. The vessels of the retina, especially the veins are tortuous. The haemorrhages are usually seen in the periphery near or over the veins. They may rarely be found around the disc and macular area is hardly ever involved. The haemorrhages are large and of varied shapes and their origin from the involved veins can be made out, though the veins are temporarily obscured by the haemorrhages. Around the veins marked perivascular

mile altitude range there are alternate periods of 45 minutes of day light, 45 minutes of night, and the pupils often will be dilated for brief exposures to sunlight

Illumination from the sun is approximately 10 000 foot candles (108,000 lux) at the earth's surface at noon in summer in middle latitudes (11) At altitudes above the atmosphere, the illumination is increased approximately 30 per cent to about 13 600 foot candles (146,800 lux) (9) We find that the irradiance in space is increased over that at sea level in about the same proportion as the solar constant going from 1.4 at sea level to 2 cal/cm<sup>2</sup>/min<sup>-1</sup> above the atmosphere an increase of approximately 50 per cent This may then result in a tendency to subjective underestimation of the retinal burn danger (13) since the sun's irradiance would increase 50 per cent while the subjective brightness rises only 30 per cent At sea level the critical time of exposure to obtain a foveal burn has variously been estimated as about one minute or less (5) In space it may result in 10 to 15 seconds in an unprotected normal eye (4, 16)

Within our own solar system the irradiance of the sun's image on the retina is independent of the distance due to the focusing power of the eye Although the size of the image changes inversely with distance the amount of energy reaching a unit area in unit time is not decreased since there is no attenuating atmosphere present Therefore even though the image size decreases with distance the critical time of exposure may remain nearly the same

In most situations retinal burns do not present as serious a possibility as the transient reduction in retinal sensitivity which follows illumination at high levels (3) If reduced sensitivity results in a pilot being unable to perform critical visual tasks promptly, the results could prove fatal The literature is filled with data on dark adaptation but most of it is not relevant to the problem of flash blindness There has been little work done to determine the sensitivity changes within the first few critical seconds or fractions of a second Recently investigators have undertaken this task (3, 10, 12, 14) This information is vital and is sorely needed for guidance in the development of protective devices

Numerous protective devices from fixed filters to self attenuating variable density photoreactive filters have been proposed Of these, the phototropic filters are the most fascinating and should they become perfected they could be utilized to great advantage in the windows of space vehicles and helmet visors of the astronauts A dependable solution is necessary not only for comfort but as a means of protection to the astronaut For example, orbital rendezvous will require intricate maneuvers and dazzle from a sudden reflection or direct visualization of the bright solar disc during final closure could be disastrous

It has been suggested that judgment of distance in space may be somewhat more difficult since some of our clues such as aerial

The year 1961 brought the pioneer orbital flights of the Russian Cosmonauts Gagarin and Titov and the suborbital flights of American Astronauts Shepard and Grissom. The year 1962, highlighted by the successful orbital flights of Glenn and Carpenter, from the United States, and the dual orbiting of Popovich and Nikolayev, from the Soviet Union, firmly established this new era of "man in space."

We, as doctors, can feel a sense of pride in the participation of medicine along with our allied sciences in helping to make this great adventure possible. Most of us are familiar with the problems of atmospheric flight and the great strides investigators have made in meeting these challenges. Most of these problems are still with us, and now with space flight new problems appear and the old ones become more complex.

Let us briefly consider this hostile environment the astronaut encounters by reviewing the various altitudes at which man requires support equipment. The visual system is particularly sensitive to oxygen lack. At only 5,000 ft (1.5 km) the first indication of decreased oxygen is manifested by diminished visual acuity at night. The symptoms of hypoxia become increasingly evident above 10,000 ft (3 km) with the corresponding decrease in partial pressure of oxygen. At 16,000 ft (4.8 km) there is a 10 per cent loss in night vision ability, and from this altitude up to 25,000 ft (7.5 km) accommodation, convergence power and fusional amplitude continue to decrease. Above 25,000 ft (7.5 km), without support, both vision and consciousness are lost and permanent brain and retinal damage can occur. At 50,000 ft (15 km) the time of useful consciousness without proper protection is 11 to 15 seconds or the time required for blood to go from the lungs to the brain. Above 63,000 ft (20 km) often referred to as the Armstrong line, the barometric pressure has dropped to 47 mm Hg, a point which is the same as the water vapor pressure of body fluids, and boiling of body fluids occurs (1). At 80,000 ft (25 km) conventional pressurized cabins are no longer effective. Beyond 110,000 ft (32 km) there is no protective umbrella against the ultra violet rays of solar radiation. Above 100 miles (160 km) sound disappears as the strange darkness of space is reached and heat transfer by conduction and convection is lost (17).

Space environment does not become apparent at any one altitude, and the gradual change is visual as well as physical. As the astronaut proceeds into space, his surroundings appear totally different. The sky above becomes a deeper blue as the atmosphere begins to thin, and with an absence of a light absorbing and light scattering medium, the overhead sky becomes completely black except for the stars. The moon and the stars appear brighter and the stars no longer twinkle (16).

Although the human eye is amazingly adaptable and performs effectively over a range of illumination of greater than 100 million to one, it does not adjust instantly. Strughold and Ritter point out that the problem of glare is more serious in space flight because of the relatively short day night cycle (15). In vehicles orbiting in the 100-500



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concern from galactic radiation solar flares and trapped radiation as found in the Van Allen belt. Since these cannot all be shielded out reasonably one must attempt to predict within limits their effect on space cabin occupants. Therefore, a combined study by the Department of Bionucleonics and the Department of Ophthalmology, at the USAF School of Aerospace Medicine, has been undertaken. This study has utilized the synchrocyclotron at the University of California Berkeley and other sources to determine the immediate and long term effects on the eye (6). The main purpose of these studies is to determine the relative biological effectiveness (RBE) of these high energy ionizing radiations.

In addition to the problems of actual space flight aerospace ophthalmology has the challenge to perform basic investigations utilizing a unique population that is relatively asymptomatic and apparently healthy. Most of our past medical knowledge is derived from patients studied in clinics and hospitals who are ill or presumed to be ill. Thus they constitute a pre-selected group and do not provide an adequate basis for studying the natural history of many diseases nor do they provide the basis of normality. Long range studies of flying personnel can provide this information. In the field of ophthalmology much valuable information can be obtained by the establishment of a tonographic repository as we have planned at the USAF School of Aerospace Medicine.

Using present and future astronauts as excellent laboratory specimens about which we have an incredible amount of data we flight surgeons, can develop information to the benefit of the practicing ophthalmologist and Mr. and Mrs. average citizen.

Dr. David Cogan in his editorial in the May issue of the Archives of Ophthalmology pointed out ophthalmology's expanding interest in an expanding universe. The vistas of aerospace ophthalmology are exciting ones. The role of the ophthalmologist in space medicine is evident and the need for his talents will continue.

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perspective which is due to atmospheric attenuation, will not be present. Glenn accurately estimated the distance of the Atlas missile from his spacecraft for short distances, as proven by an analysis of the trajectory data (8). Thus, we feel that at least for close distances accurate estimations can be made by experienced pilots. This can prove particularly important in final closing maneuvers to achieve rendezvous.

Space myopia, or empty field myopia, has been considered by some authors to be a potentially serious problem (7, 18). Many investigations have been undertaken on this problem, and I am sure many more will be performed. To date, there has been no direct evidence of difficulty by any of our pilots in orbital missions.\*

All flyers and most researchers in aviation are familiar with the problem of increased "G" forces or gravitational stress which can result in dimness of vision and blackout. This problem is well understood and well investigated, however, the problem of weightlessness was novel to all and is a result a number of controversial predictions have been made. When the astronaut encounters prolonged weightlessness, he finds an entirely new experience, and his eyes take on an added importance. Under gravity free conditions the mechanoreceptors, such as the otolith organ, the pressoreceptors of the skin, etc., do not function, and the eye is the only sense organ he can rely upon for orientation (16). Many researchers feared that the eye would not be capable of normal function in a zero gravity condition. Some hypothesized that the extraocular and ciliary muscles could be affected and result in alterations of muscle balance, accommodation, and fusion. The short periods of weightlessness of less than one minute that could be achieved in parabolic flight did not offer enough information to support or refute these speculations. Debriefing reports from the successful flights of Glenn and Carpenter indicate that there is no apparent difficulty and support the reliability of the eye in space flight. Astronaut Glenn, in his reports, stated 'Maintaining orientation was no problem, but I believe that the pilot automatically relies much more completely on vision in space than he does in an airplane where gravity cues are available' (8).

In space we are exposed to the whole range of the electromagnetic radiation spectrum of the sun, from  $\gamma$  rays of about 10 angstroms in wavelength to radio waves up to about 10 meters in wavelength. The whole range of cosmic ray particles in their original primary form and the energy with which they enter our solar system are encountered (17). Most ophthalmologists are familiar with the effects of ultraviolet rays, visible rays, infrared rays, and lower energy  $\gamma$  rays. With increased interest in space we now become concerned with the effects of high energy proton and, to a lesser extent, alpha radiations which make up the majority of the radiation of biologic

\* Personal communications

## VISUAL PERCEPTION OF MOVEMENT

by

WING COMMANDER T C D WHITESIDE M B L

*R A F Institute of Aviation Medicine Farnborough Hants*

What appears to be the fundamental factor in the visual perception of movement of an object against a featureless background is the comparison of sensations of eye movement and the sensations of movement produced by an image travelling across the retina. Thus the visual perception of movement can be determined by the movement of an image across the retinal mosaic but one must take into account also movement of the eyes for if one is tracking a moving object the image may be stationary upon the retina yet there is a sensation of movement because the eyes are changing position. To this sensation of movement is of course added the retinal sensation of movement produced by the relative displacement of the background in the opposite direction to that of the moving target. Thus if one is looking at a moving target against an untextured or otherwise empty visual field the threshold for movement perception is higher than that in which one observes a target against a textured background.

The different patterns of eye movements have now to be considered. First the fast phase. Usually eye movements made in the course of search or in looking from one object to another consist of saccades of very high velocity (about 600/sec according to Westheimer) and these are interspersed with fixational pauses. During the fast saccade there is no visual perception of any detail whatsoever under normal circumstances. The question of whether there is in fact during this saccade any retinal or central inhibition appears to have been solved by some recent experiments carried out at Farnborough in which we have shown that an electronic flash of some 10 microseconds duration can be seen during the fast phase of eye movement. In this experiment the flash was triggered off by the corneal retinal potentials so that one could cause the flash to appear either at the beginning towards the middle or towards the end of the saccade. On all occasions the flash was seen. Nor could it be suggested that what was detected was the visual after image for if this had been the case the position of the flash would have been displaced so that it appeared in line with the final fixation point. There was in fact displacement which one could attribute to the inevitable delays in the retinal processes but the

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illusion on the basis of the system diagram shown in Figure 1. This figure shows primary efferent activity arising from such factors as labyrinthine activity and giving rise to a sensation of movement as well as to an actual contraction of what we have called the 'agonist' extra ocular muscles. When the subject who fixates a small light source perceives as a result of the small retinal displacement that his fixation has drifted to one side, there is initiated a fixation reflex to centralise the fixation spot again. This fixation reflex calls for a pattern of efferent activity again but aimed at the extra ocular muscles whose action is

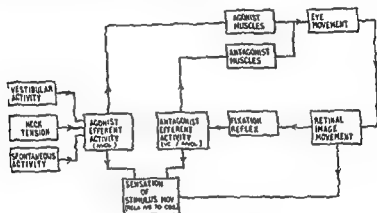


FIG. 1 (Whiteside 1963)

antagonist to the voluntarily acting group. This efferent activity pattern also gives rise to a sensation of movement and it seems that this is the sensation which dominates, possibly because the pattern of efferent activity is one resulting in small saccadic corrections rather than slow drifts and therefore having a character of bursts or volleys rather than slower changes in the frequency of the efferent volley. It is evident that in this figure the antagonist efferent activity and the associated circuit constitutes virtually a servo loop which can open simply by removing the visual stimulus and therefore the information from the misalignment detector.

Similarly it is probable that the eye movements in the oculogravic illusion give rise to a sensation of movement of the visual field upwards with increase in  $g$ . The fact that eye movement is not usually detected in observations on the oculogravic illusion may thus be due to the presence of a fixation point and therefore to the fact that the servo-loop is closed. If the loop is opened the character of the eye movements as a result of increase in acceleration becomes more obvious. It consists most frequently of a downward movement with increase in  $g$  or an upward movement with a decrease in  $g$ .

displacements caused by these delays indicated that the flash was still being seen during the first phase of the eye movement.

If there is no appreciable inhibitory change one must conclude that the visual scene is not impressed upon the retina simply because the eye is moving too quickly. Further experiments carried out with a mirror rotating at such a speed as to cause a visual scene to move at 600°/sec likewise prevented the subject from seeing any detail whatsoever, although he was, of course, able to detect an electronic flash of very short duration. There was on this occasion no apparent displacement of the flash since no eye movement was involved and therefore since there was no temporal difference in the appreciation of the retinal stimulus and of the simultaneous eye position. The experiments in which such a difference was found suggest that the retinal image takes longer to be perceived than does the information on eye position.

Thus, normally the individual sees the visual world in a series of fixational pauses during which fixed objects about him give rise to fixed images upon the retina and therefore to no movement. On such a basis it seems unnecessary to invoke more complex explanations to account for the stability of the visual world. During such fixational pauses, of course, an object moving across the visual field will give rise to an image tracked across the retina and therefore to a visual sensation of movement.

Although in scanning there are normally (in general) no eye movements sufficiently slow to enable one to see the external world during that eye movement, there are slow eye movements which occur either during the tracking of a moving object or which occur reflexly for example from labyrinthine activity. Furthermore it has been shown by Ditchburn and Ginsborg that if the eye is in darkness and at rest, it undergoes a series of slow drifts of fairly large magnitude in spite of the fact that the subject is attempting to maintain his gaze in a constant direction.

It has been suggested, that the sensation of position of the eye is associated with the size of the efferent volley (Merton 1961). Thus if the eye is displaced passively, a visual after image impressed upon the retina will seem to remain perfectly stable in front of the subject whereas, of course, the external scene will appear to move since its image is moving across the retina. On the other hand, if one makes or initiates an active eye movement, whether it be voluntary, or involuntary as a result of labyrinthine activity, a visual after image will be seen to move in the direction of the eye movement. A visual scene may appear to move in the opposite direction or to be spatially stabilised. However, if the external field of view consists only of a small light source observed in darkness, this too will appear to move but in a direction apparently opposite to that of the slow drift.

As a result of observations made in Pensacola, Florida, Graybiel and Niven and I have suggested an explanation for the autokinetic



## GENERAL CONCEPTS OF EALES'S DISEASE

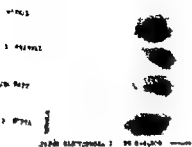
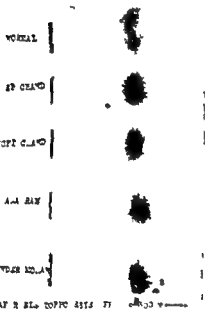


Fig 1 Showing normal haemoglobin pattern in cases of Eales's disease

2 Showing normal haemoglobin pattern in cases of Eales's disease



4 Showing normal haemoglobin pattern in cases of Eales's disease

$\gamma$   $\beta$   $\alpha_2$   $\alpha_1$  Hb

1

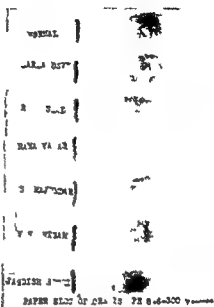
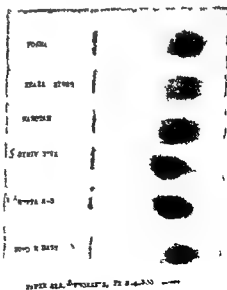


Fig 3 Showing normal haemoglobin pattern in cases of Eales's disease



PAPER ELECTROPHORESIS, PH 8.4-8.5

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Figs 1 and 2 reproduced by permission from the annals of the Royal College of Surgeons of England

Such an upward movement has been demonstrated in experiments on what has been called the elevator illusion. This refers to the apparent movement downwards of the walls of a lift when it is beginning its descent. Figure 2 shows the pattern of eye movement occurring at the onset of such a deceleration. It is evident that the eye moves upwards by some 5 in a short space of time. It is probable that the

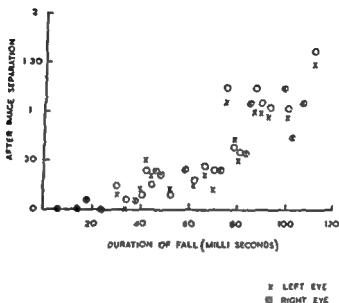


FIG 2 (Whiteside 1963) \*

presence of this eye movement in response to a step change from one to zero  $g$  is due to the fact that there has been insufficient time for servo loop to correct a fast change in the agonist activity.

To resume, it seems therefore, that we observe the visual world in a series of fixational pauses and that during these pauses any image moving on the retina is interpreted as moving. We may, however, have a slow eye movement occurring reflexly, in which case, a comparison of the rates of movement of the eye and of a retinal image likewise provides information as to visual movement relative to the observer. The presence of a pattern of efferent activity which is attempting to move the eyes may also give rise to sensation of movement when the image on the retina is fixed, as when one is observing a visual after image, or a scene which is stabilised on the retina. This sensation of movement which may arise in paralysis of extra ocular muscles due to organic or experimental causes such as the effect of curare gives rise to apparent drifts of the visual scene in the same direction as that of the attempted eye movement. It seems possible that such an explanation could be extended to take account of many other neurological conditions in which illusory drifts of the visual scene are observed.

decreased Foveal threshold was tripled(7) Brown and Burke showed that visual reaction time is increased by acceleration(8)

*Darkling or glare* may occur while traveling into the sun or above a surface which has a high reflectance such as clouds snow, or desert It may produce functional disturbance such as the loss of adaptation when a night pilot is exposed to intense searchlight beams Experimental studies of high intensity carbon arc flashes of only 0.1 second duration have shown recovery sufficient to read aircraft instruments to be as long as three minutes(9) The symptoms due to prolonged glare are headache, ocular pain and concentric contraction of the visual field Older pilots are greater affected (10) Glare becomes of increasing importance the higher one ascends At altitude, the upper atmosphere becomes increasingly deep blue due to the decreased atmospheric scattering and the lower field becomes brighter with greater glare Strughold and Ritter(11) have pointed out that in the blackness of space an astronaut with dilated pupils may experience functionally disturbing glare when he looks into the brilliant disc of the sun

*Infrared retinal burns* may be suffered at altitude unless the pilot is alert to its hazards On earth Cordes found it required one minute exposure to sunlight to produce a retinal burn(12) In space it may be less than ten seconds High speed electromechanical goggles have been developed which close in less than 500 micro seconds after a high intensity flash such as a nuclear explosion

*Ultraviolet Light* those wave lengths shorter than 3050 Å units have poor penetration and seldom produce deep ocular damage Its ill effects may be manifested as snow blindness lid edema, superficial keratitis lens fluorescence unless obviated by special filters Most of the ultraviolet radiation is absorbed by water vapor and clouds of the lower atmosphere Consequently the higher one ascends the greater the possible effects of the ultraviolet light

*Other high energy radiation* in the form of alpha and proton particles may be encountered in cosmic rays and more intensely in the area of the Van Allen Belts In the dark adapted eye these may be experienced as slashes of light by the astronaut The highly sensitive epithelium of the lens capsule is easily damaged by radiation Culver and Newton have warned against flights of long duration through these high energy belts and especially during periods of Solar Activity(13)

*Wind Blast Visual Problems* only occur as accidents either from windshield breakage or canopy ejection or from pilot ejection from the cockpit of a high performance aircraft Wind tunnel experiments have shown facial tolerance to 300 m.p.h. for 30 seconds without severe ocular damage Bail out survivors from military jet craft have endured greater wind blast stresses Goggles are unsatisfactory as at this speed they are torn off or broken Helmets or ejection capsules afford the best protection

## DISCUSSION

### PROBLEMS RAISED IN OPHTHALMOLOGY BY RECENT ADVANCES IN AVIATION

By

JOHN R. FINLAY

Connecticut (U S 1)

The ophthalmologic problems associated with modern advancement in aviation *per se* differ only in degree with those so well presented at the Ophthalmological Society of Paris, by Mercier and Duguet seventeen years ago(1) The problems related to space travel offer some new difficulties The Physiopathology of vision at altitude are largely those of anoxemia Between 5-10,000 feet, the slightly reduced partial pressure of oxygen reduces the night vision of the unsupported subject Psychomotor and sensory disturbances associated with altitude sickness may occur above 14,000 feet, Above 30,000 feet, unconsciousness and circulatory collapse will ensue McIlrland and Halperin have shown a shift of the retinal sensitivity curve with anoxemia which accounts for the gradual darkening and depression of the vision that fliers have experienced at high altitudes(2) The Stereoscopic sense and color vision are little affected by anoxemia, but there is reduction in accommodation(3) Motility, convergence, and oculomotor balance are adversely affected by lack of oxygen Night vision is mentioned as greatly depressed by anoxia Ocular tension even in the glaucomatous eye is not affected by oxygen deficiency or altitude

*Decompression effects* are largely due to argon embolism which may manifest as migrainous scotomata or hazy vision It has occurred in pilots flying at low altitude who have been previously scuba diving for recreation

*Visual troubles due to rectilinear or centrifugal forces* are dependent on the posture of the subject Nystagmus, ptosis, over convergence and grey out may develop if the subject is sitting and exposed to positive gravitational force(4) Blackout may occur after several seconds of + 4.5 G While in the horizontal position the subject may be able to tolerate + 12 G for several minutes before blackout(5) The tolerance to negative gravitational forces is much less Red out and retinal hemorrhages may occur after minus 3 G forces of short duration

*The effects of acceleration* are similar to the centrifugal forces appreciated in a horizontal position, and ocular physiologic tolerances are high At 4 G acceleration, White(6) found the visual acuity to be

Recent series of mid air collisions and near misses have resulted in a tremendous interest in collision avoidance measures. To avoid collisions the following factors should be known to a pilot about the intruding aircraft: 1 Presence and location 2 Identification 3 Heading 4 Distance or Range 5 Altitude 6 Speed 7 Attitude 8 Intended Maneuver. Investigation is continually being made to determine if exterior lighting systems, smoke and vapor trails, optical devices, or training procedures can augment any of these eight types of information. Studies at the Applied Psychology Corporation at Arlington, Virginia, have shown that pilot subjects report most reliance on apparent relative motion of a target in making their judgements about the outcome of simulated collision problems(18).

1 *Presence and Location* Ignorance of the location of an intruding target will produce probable detection distance of only 1/4 or 1/3 of the threshold range. During day the presence of an aircraft intruder may be accentuated by color schemes. In general the under surfaces of a plane should be a very dark color. The upper surfaces of the plane should be a very light hue with a high reflectance factor, and all colors sharply delineated. If broad surfaces such as the rudder are used for displays of fluorescent paint the intruding craft will be more conspicuous under many conditions(17b). At night detection is increased by high intensity navigation lights. Flashing helps but may be disorienting to both the pilot and observer. The basic concept still is valid that any constant bearing observed between the intruding aircraft and a spot on the observers windshield will indicate the existence of the potential collision(17c).

2 *The Identification of an Aircraft* will give cues as to the possibility of collision. The difference between a jet and a helicopter intruder will call for appropriate response.

3 *The Heading of the Intruding Aircraft* should be as precisely determined as possible so that a pilot can check his own course and estimate the flight path of the intruding aircraft.

4 *Range and Distance* At night estimation of range becomes a most difficult task. Some cues exist in the intensity and pattern of running lights but since at present there is no standardization in aircraft navigational lights this becomes most difficult. Aircraft bearing high intensity lights and quadrant identification signals are best detected.

5 *Relative Altitude* In most cases pilots judge relative altitude with reference to the horizon. This may be extremely difficult at night. Signal light configuration indicating altitude has met with little success. At higher altitudes estimation of the precise height of the intruding aircraft can be mislead by the attitude of the observers plane.

6 *Speed* Speed may be estimated by the type of aircraft identified.

7 *Attitude* An appraisal of the attitude of the intruding aircraft may quickly show that it is executing an avoidance maneuver, or rolling into a collision course.

**Vibration** It has been shown that the visual acuity is impaired by large amplitude vibration. Above 100 cps little change in vision was noted. The maximum effect of vibration occurs generally in the 25 to 40 cps range, and again from the 60 to 90 cps(14). These frequencies are present in modern aircraft of the propeller variety, and especially in helicopters. Vibrations of the aircraft, especially of the instrument panel produce ocular and general fatigue. These vibrations can be dampened by proper seat and instrument mounting.

**Weightlessness** There is some evidence of minimal loss of visual acuity associated with weightlessness. Pigg and Kram(15), found that there was 6% loss of acuity at 0 gravity of a 14 seconds duration. Orientation of a pilot in space craft will depend primarily on vision in the absence of reliable gravitational cues. Illusions of object displacement occur in weightlessness due to oculogyric and oculogravic reflexes(16).

**Visual Problems in Collision Avoidance** The safe occupancy of airspace depends on the ability of each pilot to maintain vigilance and take corrective action when necessary. All pilots are not of the high caliber and training as those who brought you to the meeting. The activity of general aviation accounts for the greater part of flying in the United States. General aviation covers all flying except that preformed by the public carriers, and the military, and accounts for more than three times the flying time of the air carriers in their domestic operations. Over half of the landing and departures at the larger airports and virtually all the activity at the smaller airports can be attributed to general aviation(17). The proportion of pilots who possess the ability to fly a plane with sole reference to instruments is small. The modernization of private aircraft places a single engine plane of 200 m p h at the command of pilots who may have minimal training and experience. All pilots during VFR weather must maintain vigilance for their mutual safety. Visual Flight Rules cover those flying conditions in which there is a visibility greater than one mile distance, and a cloud ceiling of over 1200 feet. The requirements for visual flying conditions about airports and in high traffic density areas and along air traffic routes is more critical. Less than these conditions necessitates the filing of an instrument flight plan. In this case separation of aircraft is the responsibility of air traffic control. However, the pilot flying on an instrument flight plan during clear (VFR, or marginal weather) may be given a false sense of security that he alone is privileged to occupy that particular air space. His vigilance may be somewhat dampened by the multitude of intra cockpit duties. More than 85% of air collisions have occurred during VFR operations. In 1960 there were 24 collisions in the United States of America. In 1961 there were 22, and in the first nine months of 1962 there were 12. Many of these accidents can be attributed to inattentiveness. Short has examined the difficulty of dividing a pilot's attention between cockpit and the exterior, in the search for intruder aircraft(17). Monitoring the cockpit reduces external vigilance in the order of 60%.

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8 The Intended maneuver of each aircraft remains the most difficult to estimate

In high traffic density areas one reasonable solution to collision danger is *en route* radar surveillance by air traffic control. This has been instituted on the Eastern Seaboard of the United States. Even with this help visualization through haze layers may be difficult. Often in the usual haze over New York, with reported visibility of over five miles I fail to see the traffic that radar assures me is only two miles away. Many pilots of far greater experience report the same difficulty.

Two types of radar help exist. Precision Radar systems provides exact 3 dimensional location of an aircraft as it approaches for a landing. However, general radar surveillance can neither intrinsically identify a target nor show its altitude. Transponders within the aircraft more frequently in the future will automatically couple this information into the radar screen below. Four types of airborne anticollision devices based on radio, micro wave or infrared transmission have been studied by the government of the United States since 1958. Due to lack of promising developments this study is being discontinued (19). Thus the responsibility for collision avoidance during VFR conditions rest on the visual capabilities of the pilot. Any ophthalmologist who treats even the occasional recreational pilot should bear this well in mind.

*Cockpit Visual Problems* For many years men have been flying aircraft which have been designed by engineers who have given poor recognition to the visual problems of the pilot. In most planes, and especially those in the air carrier classification there is restricted windshield visibility. In many cases there is only a narrow view ahead, right and left, and seldom below and to the rear. This is caused by the multitude of instruments and controls which need be placed within the pilots reach or view. Windshield wipers in many cases are inadequate. Reduction of visual acuity is partially due to the pre-empting of accommodation by unclear windshields (20). Prolonged search into an empty field also produces a functional myopia. Autokinetic illusions and vertigo trouble the untrained pilot (21).

Within the cockpit the pilot is dependent upon antiquated instrumentation which has been engineered on a Space Available basis. This has resulted in a uniform three inch diameter instrument dial, each one of which presents a single bit of information to the pilot about the complex workings of his ship.

The instruments are of stereotyped size, shape and scale, regardless of the function indicated and show many of the following faults:

*The instruments are poorly placed.* This introduces a high parallax error of the needles in certain portions of the dial for those peripherally mounted.

In one aircraft carrier, the needle and ball, a primary flight instrument is placed behind the control column so that if needed in an emergency it would be obscured.

The presbyopic captain who must read the Doppler Scale mounted ten inches above his forehead, next scan the brilliant horizon and then re-adapt to read the dim radar scope on the cockpit floor, has his visual patience sorely tried.

Poor grouping of instruments is noted especially in the light planes where instruments related to aircraft performance, engine performance, navigation and communication are scattered at random over the span of the panel.

The lighting of an instrument may be inadequate or shadowed by exterior light.

To preserve dark adaptation red light is used for panel illumination. Pilots complain that the extensive use of red light diminishes its effectiveness as a warning signal.

The warning flag indicating malfunction of a navigational device may be a small poorly illuminated red flag. Many a well trained pilot has failed his flight check and been grounded for inattentiveness to this inadequate warning.

Auditory aids in warning devices are being slowly developed. The pilot must sample 20 or 30 odd bits of information from his instrument panel in order to determine the performance of his aircraft. In the laboratory the best possible sampling rate that man can achieve probably is in the order of three instruments per second. In the aircraft this speed is impossible. Therefore scanning 20 or 30 instruments requires time. Because of the lag inherent in each instrument the information is already an historic fact. A delayed reaction period of 2-5 seconds ensues and then the pilot makes appropriate movement of his controls. At this time he must predict the final readings of his instruments and take corrective action before his aircraft arrives at its intended situation. If he does not he will have over-controlled his aircraft.

*Visual Problems of Landing* The intra-cockpit visual tasks of the pilot at take-off and landing and at all times during visual flight conditions must be superseded by the exterior visual stimuli received by the pilot. Thus even though he has monitored his cockpit instruments carefully on take-off the pilot who is unaware of a flight of stallings rising from the runway ahead meets with disaster. The need for instantaneous change from instrument to visual flight is apparent when we consider the pilot who approaches for landing at night with poor visibility. He is relying completely on instruments until the time he reaches the middle marker of the instrument landing system where he is only several hundred feet above and  $\frac{1}{2}$  mile away from touch-down. He must quickly shift his gaze from the instruments to the runway. This transition has often resulted in a misjudgement of the elevation of the runway even under the best of lighting conditions.

*Landing Systems.* To obviate these difficulties, work is progressing in two directions. The British have developed an automatic landing system in which the pilot performs only a monitoring function to insure that the landing system is functioning correctly. This system offers great promise. It has been estimated that the margin of error, of malfunction of this device is in the order of one to 10 landings for this Triplex System(22). However, it will be many years before it could be possible to install such automatic systems in even the larger airports of the world. In another direction there is work being done to reflect a simulated runway and instrumentation on a half mirrored surface directly on the windshield. The pilot can control his plane by collimated instrumentation and by the external visual cues which will appear as he lands. This type of system promises to be less costly and be able to be used in remote and poorly equipped airports throughout the world. This method of interpretation of flight information would be the same in IIR flight as in VFR flight and transition error is virtually eliminated(23).

Considering the visual and other problems of the pilot in the atmosphere one may question whether man can efficiently safely control space craft. Compared to automatic systems, the human pilot has a slow response, is subject to greater error and fatigue and requires food and sleep. At the Institute of Aerospace Science Meeting in Seattle, the relative efficiency of man and machine were compared. It was felt, largely, that the machine should be the performer and the role of man relegated to monitoring and decision making. Robert Gilruth, Director of Manned Space Center of National Aeronautics and Space Administration, however, showed that considering weight, space, cost and reliability, a manned system would be superior to a fully automatic system.

This return to manual control of flight is considered the greatest advance the Gemini and Apollo capsules will make over Mercury missions. The successful piloted flights of Shurra in Sigma Seven and of the near rendezvous (63 miles) of Colonel Popovich and Major Nikolayev have ably demonstrated this capability.

Once again the visual potentiality of man will be subject to the greatest test. In all aeronautic endeavors the knowledge of man's physical limitations has served to stimulate engineering developments which have complimented his capabilities. Thus the coordinated efforts of the Engineer, the Pilot and the Physician can eventually surmount problems of modern aviation.

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Eales's disease has also been ascribed to the hormonal disorders like hypopituitarism<sup>(20, 21)</sup> and relative deficiency of androgens. We have not done any hormonal assays but therapy with androgens has given equivocal results suggesting indirectly that deficiency of androgens is probably not a causative factor.

Deficient oxygen carrying capacity of the blood may affect the capillary walls of the retinal blood vessels leading to retinal and vitreal haemorrhages. We estimated the oxygen concentration by Van Slyke's method in 50 normal individuals and 50 cases of Eales's disease of the same age group. Our observations do reveal that in a majority of cases of Eales's disease the oxygen concentration of the blood was subnormal (Table II). This deficiency probably leads to venospasms, oedema of retina, increase in fragility of small capillaries and greater permeability of venules and exudation.

The aetiology of Eales's disease is as yet uncertain and remains conjectural. Deficient oxygen carrying capacity without sickling of RBC is an important finding and the factors producing this deficiency of oxygenation require further experimentation.

#### CLINICAL PICTURE

The disease is conventionally described to be present in apparently healthy young males. In this series only two cases were seen in females and the rest were males. The minimum age in this series was 18 years and the maximum age was 45 years. Those in the later age group came in 4th or 5th attack. The average age of the onset of the disease has been 23 years.

Eales had pointed out that in most of the cases the L.E. is affected earlier than the right eye and this observation is fully supported by our series as in 32 of the 50 cases either the left eye was the only involved eye or it was affected earlier than the right eye.

The patient complains of a sudden painless blurring of vision on awakening in the morning. The degree of blurring depends on the extent of haemorrhage and the vision may even be reduced to perception of light. One eye is involved earlier than the other but eventually both eyes are affected. The ophthalmoscopic picture depends upon the severity of the haemorrhage. If there is massive haemorrhage in the vitreous fundus reflex is absent but a black or faint red reflex may be seen. If the haemorrhage is minute and the patient complains of only few black spots in the visual field, the vitreous may look clear and haemorrhages can be seen in the retina. Intermediate grades of haemorrhages in the vitreous may be visible. The vessels of the retina especially the veins are tortuous. The haemorrhages are usually seen in the periphery near or over the veins. They may rarely be found around the disc and macular area. They are hardly ever involved. The haemorrhages are large and of varied shapes and their origin from the involved veins can be made out though the veins are temporarily obscured by the haemorrhages. Around the veins marked perivascular

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roentgen equivalent, man (REM) It is the same with gamma rays, but the relative biological effectiveness (RBE) value is one It is the same with thermal neutrons as it is with gamma rays except that it is five REM and five RBE value Fast neutrons have a REM of ten, and RBE value of ten and protons have a REM of ten and RBE value of ten Alpha particles however, have twenty REM to a REP and twenty as the RBE value The establishment of permissible dose, permissible dosage rate and permissible amount of radioactive material deposited in the body is dependent on the results of biological investigations and past experience Sufficient experience has been accumulated with gamma rays and X rays up to about a million volts, so that the permissible dose and permissible dosage rate are quite definitely known In the case of radiations in space there has been much less experience Permissible amounts of radioactive material deposited in the body have not been exhaustively investigated for all radioactive isotopes Even in the case of X rays and gamma rays the long term genetic effects are not known with certainty There is good reason therefore to introduce liberal safety factors

The primary aim of all radiation protection procedures is to reduce radiation exposure to below permissible amounts Radiation hazards fall into two classifications (1) Those hazards in which there is a possibility of radioactive material entering the body and (2) those hazards in which there is a possibility of external radiation only

Electrical apparatus in which high voltages are employed is not considered a source of harmful radiation when in use However one should assume that such apparatus represents a potential hazard until it is established otherwise

With reference to alpha radiation except in the case of alpha particles from high energy accelerators there is no problem in protecting the eye from such particles originating outside the body since the energy from them is reduced to zero by a few centimeters of air or a few millimeters of solid material However since they are particularly hazardous inside the body it is necessary to use suitable equipment designed to evaluate the hazard due to contaminated air or surfaces

The problem of shielding the eye from external beta radiation is not formidable Reasonable thicknesses of solid material will obstruct all beta particles emitted from radioactive isotopes One should not overlook the fact however that secondary X rays are produced in the shielding material by the action of beta particles on matter Such X rays are more penetrating than primary beta particles and they become a significant safety hazard where high intensity beta sources are in use Therefore every installation should be checked with appropriate measuring equipment to determine the overall effectiveness of the shielding

Lucite or a similar plastic is a convenient transparent shielding material easily fabricated The thickness of air necessary to stop all beta particles of a given energy is of interest where unshielded beta sources are being handled The hazard occasioned by the introduction

## OPHTHALMIC PROBLEMS IN AVIATION

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This discussion is limited to protective measures for the eye in space. Nuclear emanations can produce harm from a distance. All of the means of shielding the eye in space flight are considered. The type of clothes, goggles, and other protective measures are related. Biologically a sufficient quantity of radiation is the amount of energy that can be absorbed per gram per disintegration under a given set of conditions. The radiation measuring instruments in use today depend on the ionizing properties of radiation for their operation. Studies are now being carried out throughout the world to decontaminate persons exposed to sudden acute effects of radioisotopes. The type and amount of medication to be used will be based on monitoring of urea. The first of these medications will be in the form of excretory stimulants, later drugs will be developed to change the chemistry of gamma emitting substances.

We know now that man can travel a few hundred miles from the earth and stay a few days in space. Although a short period of weightlessness has no deleterious effects on the eye we are not certain about effects of a longer period. We can expect deterioration of the optic nerve, retina, and extraocular muscles. If man moves out further he will have to protect the eyes from effects of corpuscular radiation. Perhaps some device will be developed which can be included in a space capsule that will counteract weightlessness.

Light clothing is known to absorb less heat than dark clothing. Goggles should be leaded and darkened, leaded and protective aprons should be worn.

Biologically, the significant quantity of radiation is the amount of energy that can be absorbed per gram per disintegration under a given set of conditions. The radiation measuring instruments in use today depend on the ionizing properties of radiation for their operation. The more common are the ionization chamber, the proportional counter, and the Geiger Muller counter. In all three types of detectors, the essential features are two electrodes across which an electric field is applied in an appropriate gas or mixture of gases. A typical instrument consists of two oppositely charged electrodes placed in an ionization chamber. Chambers should be air wall equivalent.

Reports of dosimeter readings provide a basis for estimating exposure and for adjusting plans accordingly. The readings indicate when exposure or no exposure should be avoided, and thus can also be used as a basis for controlling the exposure of the eye.

One roentgen of X rays equals one roentgen equivalent, physical (of energy absorbed) (REP), the amount of biological damage is one



The concept of radiation injury is not new. Sunlight is an example. Man has known about the effects of sunlight for a long time. He has known about the effects of fire. There are sensory warnings for light and fire. There is, however, no sensory warning for gamma radiation. Man made detecting devices must be used to help in this problem. Radiation damage is not immediate as it is with fire or sunlight.

Nuclear emanations can produce harm from a distance. Germs cannot do that. They must enter the body. Sunlight may cause harm from a distance, but its effects at the time that it is being received are known to the senses. The characteristics of radiation hazards are the following: Lack of perception by the senses, a delayed effect, and ability to penetrate thick solid material. The permissible dose of radiation is the main criterion in the measurement of safety, and there are three factors over which one has control. These are distance, time, and shielding. Distance follows the law of the inverse square. Time has maximum safe time as the basis, and shielding attenuates the radioactive power of a substance. To understand the hazards of radiation, the constituents of matter must be understood.

From the standpoint of the biological effect of neutrons upon the eye, two actions are important. These are the processes of absorption and scattering. Thermal neutrons cause a stable isotope to become radioactive on exposure. Since neutrons and hydrogen nuclei are of about the same mass, the result of an elastic collision between two such particles will be the loss of roughly half of the neutron energy. Radioactive isotopes may disintegrate by several methods, one of which is the ionization method of interaction of radiation with matter. In this method, a neutral atom splits into positive and negative parts. Matter in the solid, liquid, or gas state can be ionized by charged particles provided they possess sufficient energy to eject electrons from the particular atom or molecule under consideration. Biological damage due to radiation is a consequence of ionization in the body tissue.

Three types of interaction between photons and matter occur:

- (1) Photoelectric effect
  - (2) Scattering (this has two varieties, the Compton type and the coherent type)
  - (3) Pair production
- In the photoelectric process, all of the energy of the photon is transferred to an inner orbital electron of an atom. In the scattering process, there is:
- (a) the Compton type, in which the photon may collide with an electron and impart part of its energy to it, and
  - (b) the coherent type, where the photon bounces off the atom or molecule changing direction without losing energy.

The following points must be considered. For alpha and low beta radiation, the damage would produce a large dose in the deeper layers of tissue. 1 roentgen equals 83 erg absorbed per gram of air. In soft tissue, the amount of energy absorbed per gram is approximately the same as air. Units of measurement based on time are roentgens per minute and milliroentgens per hour.

Rubber gloves, protective clothing, and nonabsorbent footwear should be worn. In case there is danger from airborne contamination,

of beta emitters into the body necessitates the use of sensitive detection equipment in evaluating the hazard due to contaminated surfaces and to contaminated air.

The fundamental purposes of protective measures in handling radioisotopes are the following: (1) To prevent ingestion, inhalation, and interstitial or other modes of entry into the body; (2) To reduce the amounts of external irradiation to permissible levels. There is a wide difference in the hazard created by absorption of various radioisotopes into the body. Doses of radium and plutonium that are currently considered safe are radium, 0.1 microgram fixed in the body, and plutonium, 0.3 microgram fixed in the body. Where sources are of low intensity the danger to the eye is not great. Even for small amounts of activity it is often necessary to fabricate protective modalities to fit a specific situation. In the effort to increase the distance between the eye and the source of radiation, care should be exercised in the design of shielding equipment. Procedures employing new tools should be rehearsed with inactive material before work with active material is begun.

The fundamental purpose of protective measures in dealing with sources of radiation which represent an external hazard only is to reduce amounts of external radiation to permissible levels. If the eye is exposed to more than one type of radiation in a given weekly period, the total exposure from all components should not exceed 0.3 RLM. In the case of exposure of the eye and forehead to various types of radiation, the total dose from all components should not exceed 1/5 RLM in a given period of one week.

Under certain conditions, a vacuum tube can produce x-rays of considerable intensity. Any device in which electrons are accelerated is a potential source of x-rays and should be checked in operation to determine if a radiation hazard exists.

In general, devices employing high accelerating voltages and high electron currents are potent x-ray sources. The biological manifestations or symptoms due to either external or internal low level radiation exposure may be delayed for long periods of time. This renders the immediate estimation of damage difficult. Present practice consists of following the person's physical condition by conducting a complete physical examination before, during, and after work with sources of radiation.

The decontamination of a surface that has been contaminated with radioactive material is a very difficult procedure. In many cases it is advisable to remove that part of the surface that has become contaminated and treat it as radioactive waste. This is especially true of porous surfaces because it is next to impossible to decontaminate them completely. If the type of work being done requires quantitative counting of samples, the tolerable contamination may be smaller than the permissible level recommended for personnel protection.

Correlation between the static and kinetic visual acuities of 86 D pilots and police officers of the highway patrol was measured. This data indicates that the static and kinetic visual acuities are not always proportional. Both visual acuities of ordinary civilians differ more markedly than those of a man in specialized profession. A comparison of this data with that in the preceding data emphasizes the superior kinetic visual acuity of the jet pilots.

The kinetic visual acuity of a subject decreases in proportion to an increase in the velocity of the moving object that is being viewed. In this result individual differences also may be recognized.

After fatigue was introduced by subjecting the subject to a physical work load, the kinetic visual acuity of the subject decreased noticeably, especially at the higher velocities of the visual object. This tendency also can be observed when the subject is suffering from lack of sleep, mental exhaustion, and so on.

The variation in the kinetic visual acuity of a pilot before and after a flight in a jet plane was noticeable. Although the decrease in the kinetic visual acuity after each flight is slight, repeated measurements show a gradual decrease in the acuity; therefore the decrease in the pilots' kinetic visual acuity is not recognized by the pilots themselves because their static visual acuity remains the same.

The correlation between the kinetic visual acuity of pilots and their self-determined appraisals was proportional, though only a few pilots had been interviewed. The same correlation was seen in police officers of the highway patrol. The officers having a poor kinetic visual acuity usually have poor records and have accidents more frequently.

As was previously mentioned, the kinetic visual acuity is an important function of the eye for pilots, and we believe that our Kinetic Vision Tester will play an indispensable role in a quality test for a pilot in the detection of his physical condition and in the measurement of his fatigue.

Several factors in the physiological mechanism concerning the difference between the static and kinetic visual acuities are presumed, namely, that the speed of accommodation and the minutely accommodative oscillation, a term which have recently coined, may take a part in the production of kinetic visual acuity.

The amount of time necessary for a subject's eye to accommodate on an object directly in front of him at distances of from five to thirteen meters was measured, and indicated that the accommodation time was proportionate to the visual distance rather than to the accommodative amount.

The experiments were performed in such ways that the moving object was exposed for a short yet constant time, and during that time the perceptible limiting distance was measured in two methods. The one shows the results when the exposure apparatus was attached to the visual object part, and the other showed the data when the exposure

properly designed respirators should be employed. Airborne contamination can be minimized by keeping the surface moist. No person must be exposed to more than 0.01 microcuries per liter by air inhalation. Particulate matter (Carbon 14) can also be filtered from the exhaust air. Not more than two curies of radium, plutonium, or other members of the radium family, and not more than 11 disintegrations per second of all other radioactive materials may be packaged in one outside container for shipment by air except by special arrangement. There must be no leakage. Studies are now being carried out throughout the world to decontaminate persons exposed to sudden acute effects of radioisotopes. The type and amount of medication used will be based on monitoring of uric acids in space flights. The first of these medications will be in the form of excretory stimulants. Later, drugs will be developed to change the chemistry of gamma emitting substances.

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## ABOUT THE IMPORTANCE OF KINETIC VISUAL ACUITY AGAINST ABILITY FOR PILOT

SUZUMURA AKIHIRO

Research Institute of Environmental Medicine  
*Nagoya University, Japan*

It is a fundamental necessity that pilots must be able to see moving objects clearly and quickly. Hitherto it was supposed that the difficulty experienced in seeing a moving object was due to the fact that the object moving, depending on various visual functions and in particular on the visual acuity of the object at rest.

From the results of many experiments we have come to the conclusion that 'seeing' a moving object cannot be explained merely by seeing the static object, that is the object at rest, but that it depends upon another visual function which differs from the function involved when seeing the static object. We have named this new visual function Kinetic Visual Acuity. This term indicates the central or parafoveal visual acuity for a moving object that is approaching in a plane perpendicular to the transverse axis of the eyes. We also have been able to produce a new apparatus for measuring Kinetic Visual Acuity which we have called a Kinetic Vision Tester.

Now, we shall discuss several facts relating to how the perceptibility of a moving object is important to pilots.

The subject, by using the optical system, can see the object that is approaching the eye in a plane perpendicular to the transverse axis of the eyes from one to twenty meters at various velocities.

Correlation between the static and kinetic visual acuities of F 86 D pilots and police officers of the highway patrol was measured. This data indicates that the static and kinetic visual acuities are not always proportional. Both visual acuities of ordinary civilians differ more markedly than those of a man in specialized profession. A comparison of this data with that in the preceding data emphasizes the superior kinetic visual acuity of the jet pilot.

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exudations varying from narrow parallel sheathing to extensive extravasations, occur. Generally one sector of the retina is believed to be involved. As the disease progresses the haemorrhage in the vitreous gets absorbed but before the vitreous has completely cleared up another haemorrhage occurs. The duration between two attacks increases, the haemorrhages become less frequent and they may cease altogether. The phase of recurrent haemorrhages is either accompanied or followed by neovascularization and development of irregular and new anastomotic channels. Ultimately retinal fibrous proliferation, retinitis proliferans and traction retinal detachment complete the sad story resulting in permanent blindness. In 11 cases the patients came with history of blurring of vision. On ophthalmoscopy the vitreous was normal and no apparent abnormality of the retina was seen, except that there seemed to be a small discontinuity in one or more of the retinal veins. Sometimes one of the main branches, while at others a smaller branch of the retinal veins showed this discontinuity (Fig. 6). These cases were not diagnosed as cases of Eales's disease. Later these cases came with a typical attack of Eales's disease (Fig. 7). This gave us a lesson that if in a susceptible case one encounters fullness and tortuosity of veins with evidence of discontinuity in their course, the cases should be diagnosed as one of Eales's disease and an adequate therapeutic regime should be enforced.

In 29 cases where the patient complained of symptoms only in the affected eye, an ophthalmoscopic examination of the other eye revealed the presence of retinal haemorrhages in the periphery in one or more quadrants. These cases eventually progressed to vitreous haemorrhages. It seems, therefore, that the haemorrhages at first are confined to the retina but eventually a haemorrhage of sufficient magnitude occurs to burst through the internal limiting membrane to find its way in the vitreous. This also suggests that a careful search for any evidence of periphlebitic reaction should be made in the apparently normal eye in Eales's disease.

In our series we have seen that in 42 cases more than one vein was involved (Fig. 8) and in several of these cases at least one small vein was involved in each quadrant (Fig. 9). We are quite certain that if careful scanning of the fundus of Eales's disease is made most of the cases will show multiplicity of periphlebitic reaction. The multiplicity of lesions may account for the failure of surgical measures adopted in this disease. We feel that the disease is revealed in 4 stages:

- I A stage of venous dilatation tortuosity and discontinuity which may be due to an anoxic venospasm
- II A stage of organic changes in the veins leading to periphlebitic vascular response and retinal haemorrhages
- III A stage of recurrent vitreous haemorrhages and
- IV Stage of retinal gliosis, retinitis proliferans, traction detachment and complete blindness

the examination of their flight possibilities at different high altitudes. These tests consisted in subjecting them in the barochamber to depressions corresponding to the following altitudes: 5 000, 12 000 and 15 000 m, and then after the ground training test in a height compensating costume they are subjected in the same costume, to depressions corresponding to the altitudes of 14 000, 16 000 and 18 000 metres. Starting from 12 000 m oxygen was administered. These seven tests were carried out each on a separate day, with a two days rest between the tests.

During these tests our examinations were systematically centered on the aspect of retinal vessels, minimum blood pressure in the central retinal artery, pulse, general arterial blood pressure, comparatively before and after entering the barochamber, during the stay in the barochamber at various time intervals (always the same for the same altitude) and immediately after the egress from the barochamber, a situation somewhat equivalent to landing. We mention that the examination of the eye fundus even during the hypopressure in the barochamber was carried out through the 2.5 cm thick visor of the barochamber to which the aviator approached his eye as much as possible just as we did with the ophthalmoscope. We may also mention that the retinal and general blood pressures have been recorded before the aviator entered the barochamber and immediately after his egress from it.

The tests were carried out on 54 aviators between the age of 21 and 35. These tests totalized 2 406 examinations in all the above mentioned experimental variants.

#### THE RESULT OF RESEARCHES

The researches have yielded the following data:

1 *The aspect of the retinal vessels.* A generalized and transient rapid retinal arteriolar spasm sets in at visibility limit with the increase in the calibre of retinal veins. At the end of the 5 000 m test the venular dilatation remains unchanged for yet another short time after the egress from the barochamber which coincides with Mercier and Duguet's (3) observations which show that subjecting young men to fictitious altitudes of 6 000 m obtained in a barochamber, a retinal vasodilatation was ascertained.

Generally in all the tests necessitating the administration of oxygen together with the discreet sustained spasm of retinal arterioles and the retinal venular dilatation a spontaneous pulse appears in case it does not already exist or it is being accentuated in case it normally and discreetly pre-exists. This situation becomes more evident in the case of ascents necessitating the administration of oxygen.

2 *The minimum retinal blood pressure.* On the ground (before entering the barochamber) it was generally comprised between the normal ground limits of 25-30 mm (Baillart) while after the egress from the barochamber it had increased with the height of the ascent being generally comprised between 40-65 mm (fig. 1, 2, 3, 4).



apparatus was attached ocular part however, in the latter case no measurement could be obtained. Thus, it may be said that accommodative speed to follow the movement of the object is necessary in order to have kinetic visual acuity.

The police officers after highway patrol duty experience a prolongation of their accommodation time and that the accommodation time of the officers having a low kinetic visual acuity is twice that of those having a good acuity. It also shows that as the kinetic visual acuity becomes lower the accommodation time increases.

From these results it may be presumed that in the production of kinetic visual acuity, whether it be high or low, the speed of accommodation and the minutely accommodative oscillation are factors which play an important role.

## RETINAL ANGIO DYNAMIC ASPECTS IN CONDITIONS OF HYPOBARISM IN HIGH ALTITUDE PILOTS

M. CARAPANCIA, M. POPESCU, I. PINTILII, M. STOIAN  
and ST. MIHAI  
(Roumania)

The visual apparatus is in a position to point out, at a detailed investigation, and by the disturbance of the delicate mechanism it consists of, not only the degree of local ocular disorders but especially—and this fact constitutes a preoccupation in the functional state of the entire organism—the ocular response to general reactions, under this latter aspect, by their graduated precision, ocular modifications adopt the aspect of a real biological titration of the complex behaviour of the organism.

The retinal arteriole, endowed with a much more voluminous wall, in comparison to its blood column, achieves the reverse of the situation of the humeral artery, in which the blood column predominates over its thin wall. Hence, it results that the humeral artery only records the blood pressure at a certain moment, while the retinal arteriole also and simultaneously records the parietal tonus which brings about visible ophthalmoscopic modifications, indicating past and present hypertensive stages, with their evolution.

In our researches we intended to examine whether and to what extent the retinal vessel can be modified in conditions of hypobarism in the barochamber, equivalent to the flight at various high altitudes.

### RESEARCH TECHNIQUE

The researches were carried out at the Aviation Medical Center during the tests to which aviators are normally subjected in view of

The phenomena observed in aviators during hypopressure resemble to those pointed out by one of us in the rabbit subjected to hypobarism(2). In those researches it is shown that hypobarism induces a rapid retinal and carotidian arteriolar spasm followed by a stable retinal and carotidian arteriolar dilatation accompanied then by the respective venular dilatation. No doubt that the phenomena observed were due to the experimental hypopressure permitted on the experience animal which succumbed immediately after.

Of interest is the parallelism of experimental phenomena identical to a certain point with the clinical ones.

As a matter of fact these experimental findings were confirmed by the still unpublished researches carried out by Acad. Prof. Gr. Benetato and co-workers which have established, by the Rein and Gibbs's method of recording the circulatory flow, the increase in the cerebral circulatory flow. What we have shown is equivalent to the increase in retinal circulatory flow both experimentally, in the animal and clinically in the aviators.

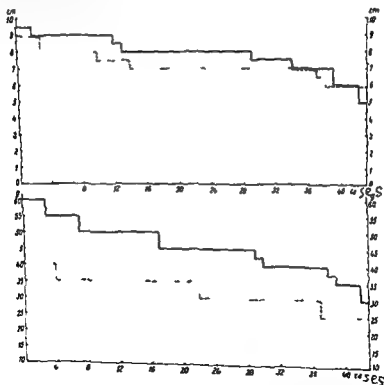


FIG. 2

Above Minimum humeral arterial tension Below Minimum retinal tension  
On the ground (broken lines) and after the hypobaric test at 12 000 m (continuous line)

3 *The pulse* It grew proportionally to the altitude, between 76-100-120/min

4 *General blood pressure* As against the ground one, after the ascent, it seldom maintained itself at the same level. In general it rose slightly

### INTERPRETATION OF RESULTS

We have shown that altitude hypopressure induces a fine, discreet, rapid, generalized and transitory arteriolar spasm at the limit of visibility, for the altitude of 5 000 m, and a constant one at altitudes which necessitate the administration of oxygen simultaneously with the arteriolar spasm appears a stable, consecutive, venulous dilatation, and usually a spontaneous venous pulse or its exaggeration in the case of its normal pre existence. The return to the ground brings about, after a few minutes, the disappearance of the venous phenomenon.

The spontaneous venous pulse, however, becomes much more evident in ascents necessitating the administration of oxygen.

These phenomena which occur at the level of retinal vessels, the smallest terminal ones, which can be directly investigated and which are anatomo physiologically equivalent to those of the central nervous system render the eye fundus examination as valuable as an indirect cerebroscopy.

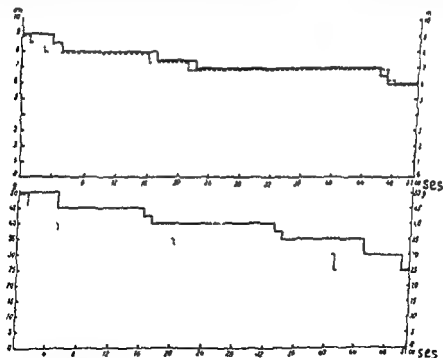


FIG 1

Above Minimum humeral arterial tension, Below Minimum retinal arterial tension. On the ground (broken lines) and after the hypobaric test at 5 000 m (continuous line)

The phenomena observed in aviators during hypopresure, resemble to those pointed out by one of us in the rabbit subjected to hypobarism(2). In those researches it is shown that hypobarism induces a rapid retinal and carotidian arteriolar spasm followed by a stable retinal and carotidian arteriolar dilatation accompanied then by the respective venular dilatation. No doubt that the phenomena observed were due to the experimental hypopresure permitted on the experience animal which succumbed immediately after.

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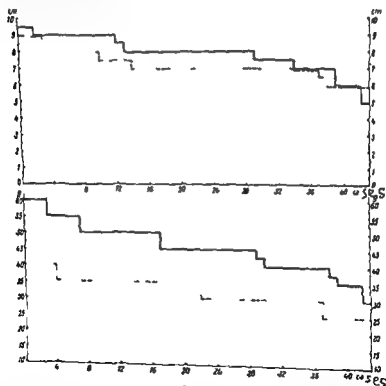


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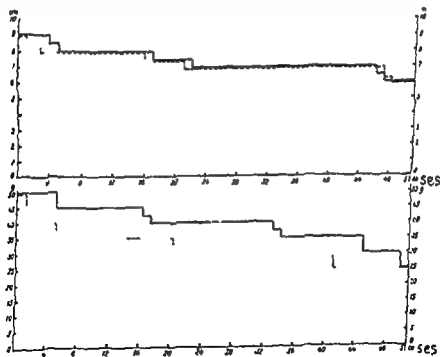


FIG 1

Above Minimum humeral arterial tension. Below Minimum retinal arterial tension. On the ground (broken lines) and after the hypobaric test at 5 000 m (continuous line)

Which is the explanation of the rapid arteriolar spasm which precedes the established vasodilatation—for the duration of the hypopressure and subsequently extended for a short time—in the eye fundus?

The explanation should be looked for in the fact that the intraocular physiology is strictly dependent upon the nutritive requirements of the retinal cell. Because of it the abnormally increased blood flow as against the nutritive requirements of the retina obligatorily determines from the very beginning a defence reaction manifested by the arteriolar contraction which impedes this surplus after which however the decompensation phenomenon of vasodilatation takes immediately place.

What is the explanation of the venular dilatation in general and of the spontaneous pulse in particular, as well as its exaggeration in the ascent necessitating the administration of oxygen?

It is known at present that an excess of oxygen induces the spasm of the retinal arteriole.

It seems easily understandable that a slight excess of oxygen induces the discreet spasm of retinal arteriole with a subsequent stasis in the retinal venules. Concomitantly the ophthalmotonus, reduced at high altitude permits the passive increase in the calibre of the retinal venula and favours at the same time the increase in the venous pressure above that of the intraocular pressure which leads to the appearance of the spontaneous venous pulse. The explanation of this phenomenon in the conditions of our researches must be looked for in the fact that the interocular pressure increases during the systole and flattens the venous wall situated under its own reduced pressure while in diastole in which conditions are reversed the vein distends returning to its normal calibre.

Thus in aviators the venous pressure is situated to the interocular pressure in conditions of a normally unstable equilibrium which imparts to the vascular wall rhythmic pressures from without inwards (intraocular pressure) and from within outwards (venous pressure). The exaggeration of the spontaneous venous pulse in the case of its normal pre-existence is due to the fact that the relation between intraocular and venous retinal pressures are of a nature allowing the equalization of the flattening and expanding movements of the venous retinal wall.

The disappearance of the spontaneous venous pulse shortly after the return to normal ground altitude is due to the fact that on the one hand oxygen ceases its action and on the other that ophthalmotonus returns to its normal conditions previous to the ascent when it was constantly either higher or lower as compared to the retinal venous pressure a situation in which the venous pulse does not appear.

The minimum retinal pressure was raised which shows that though the aspect of the retinal artery is normalized as seen on the ophthalmoscope there still existed a short time after the return to

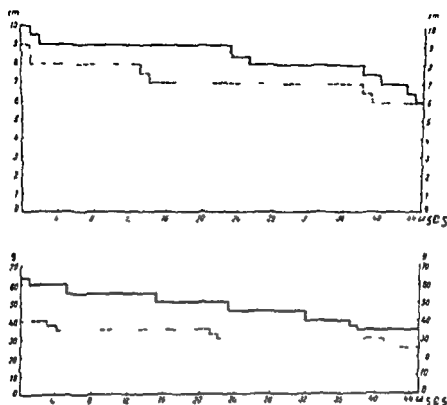


FIG 3

Above Minimum humeral arterial tension Below Minimum retinal arterial tension  
On the ground (broken lines) and after the hypobaric test at 15 000 m  
(continuous line)

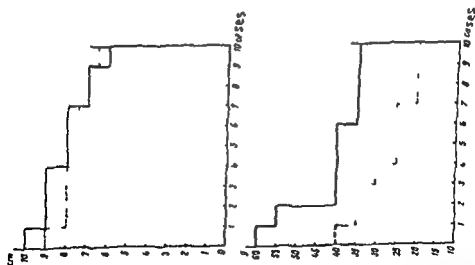


FIG 4

Above Minimum humeral arterial tension Below Minimum retinal arterial tension  
On the ground (broken lines) and after the hypobaric test at 18 000 m  
(continuous line)

In this connection we must underline the fact that our present point of view in considering the angio retinal modifications, included completely among the disturbances of the cardio vascular apparatus is no doubt, generally speaking justified

However, the existence of an eventual individuality of the cephalic vascular sector might modify fundamentally our point of view in connection with the functional phenomena of this region during general arterial hypertension

This hypothesis has been suggested by the results of the complex researches carried out by Acad Prof Gr Benetato and co workers in 1956(1) on the variations of the circulatory flow and the cerebral oxygen consumption in the dog in relation to the general circulatory flow and the total consumption of oxygen under the action of various drugs. The findings of these researches regarding the action of atropine and of histamine argue against the conception which predominated for a long time in physiology and clinical pathology, according to which the cerebral circulation is passively regulated only by the variations which occur in the general circulation at the same time they plead for the ununiform repartition along the vascular tree of the tonic sympathetical parasympathetical action with the predominance of the parasympathetic tonus at the level of the cerebral vessels

The Laboratory for Clinical and Experimental Physiology and Physiopathology of the Eye of the Normal and Pathological Physiology Institute Daniel Danielopolu - of the Academy of the Rumanian People's Republic

Director of the Institute Acad Prof Dr Gr Benetato

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#### MODIFICATIONS OF THE VISUAL ACCOMMODATION IN CONDITIONS OF HYPOBARISM IN HIGH ALTITUDE PILOTS

by

M CARAPANCEA M POPESCU, I PINTILIE M STOIAN,  
V TEODORESCU and M STEFAN

(Roumania)

Present flight conditions induce in aviators two states of myopia anoxemic and altitude or spatial myopiae. *Anoxemic myopia* — occurring



conditions of normal, ground, pressure, and slight increase in pressure, which sometimes coincides with the increased general pressure. We used the expression *sometimes*, and underline this fact, which signifies that the cephalic segment blood pressure in writers, as still on the ground, in conditions of hypertension and subsequent local stasis, is against the rest of the organism subjected to a normalized blood pressure.

### PRACTICAL CONCLUSIONS

Vascular modifications of the eye fundus, induced by altitude hypopressure still persist, a short time after the return to normal, ground pressure.

The only immediate action which venous intraocular stasis can have, in the meantime, upon any of the functions of ocular viscera is that upon the activity of the ciliary muscle.

In fact, so long as the interocular venous stasis lasts, so does undoubtedly also the one in the musculo-vascular region of the ciliary zone, and more precisely of the portion of ciliary process.

It results that the venous stasis in the ciliary muscle can but only hinder the normal functioning of the latter, i. e., hinder to a certain extent the amplitude of its normal contraction.

This situation is particularly accentuated in the case of the hypermetropic accommodation, which has a permanent character. In fact the accommodation of the hypermetrope is the expression of continuous modification of the refraction of the crystalline lens to any distance — since *punctum remotum* is virtual and placed beyond the infinite, while *punctum proximum* is placed behind the retina — subsequent to states of graduated contraction — relaxation of the ciliary muscle, transmitted by the intermediary of Zinn's zonule to the crystalline capsule, so that the eye's image be formed *always, mathematically on the retina*, starting from infinity to a distance of a few centimeters from the eye.

Thus, the writer cannot accommodate in normal conditions during the landing operation of the very rapid modern aeroplane, when the pilot is obliged to adjust both the image of the ground which approaches very rapidly, and the image of the board apparatus placed at a constantly fixed distance.

In any case, in view of the above considerations, the systematic investigation of the pressure in the retinal artery becomes compulsory, both in engaging navigating pilots and in periodic medical controls of barochamber tests, they are submitted to.

Thus, since present researches have underlined the fact that on the ground the minimum retinal blood pressure has maintained itself raised in a normal ophthalmological field and in a normal general tensorial state, hence the deduction that on the ground, the blood pressure of the cephalic segment was still in a state of hypertension as against the rest of the organism submitted to a normalized vascular pressure.

XIX CONCILIUM OPHTHALMOLOGICUM

# ACTA

*(Under patronage of the Government of India)*



VS Showing involvement of one  
vein in each sector  
Fig 9 (VS)



PCT Showing involvement of  
two big veins  
Fig 8 (PCT)



AS Later in an attack of  
Haemorrhage along Superior  
Temporal Vessels and in  
the vitreous  
Fig 7 (AS)



AS Showing Discontinuity of  
Superior Temporal Vein  
Fig 6 (AS)

In our researches we intended to find out whether and to what extent may visual acuity be modified in conditions of barochamber hypobarism equivalent to the flight at high altitudes

It is important that this phenomenon be studied since in present flight conditions it represents for the aviator the essential element in piloting the plane

#### RESEARCH TECHNIQUE

Researches were carried out at the Medical Aviation Centre during the tests to which aviators are normally subjected in view of examining their flight possibilities at different high altitudes. These tests consisted in submitting them in the barochamber to depressions corresponding to the altitudes of 5 000, 12 000 and 15 000 metres and then after ground training tests in a height compensating costume they are subjected in the same costume to depressions corresponding to the altitudes of 14 000, 16 000 and 18 000 metres. These seven tests have been carried out separately with an interval of two days between them

During these tests we have followed systematically the achromatic and chromatic static and dynamic visual accommodation of the comparative *punctum remotum* before entering the barochamber during the stay in it at various intervals (always the same for the same altitude) and immediately after the egress from the barochamber a situation somewhat equivalent to landing

The visual accommodation in the variants shown above has been investigated by the intermediary of some black and coloured letters of various dimensions corresponding to various hypernormal and normal visual acuities fixed on a paper band rotating on a kimograph at a speed of 500 mm/sec. This kimograph was placed at the prescribed distance for determining visual acuity. The examination of the perception of letters was also followed in barochamber hypopressure atmospheric conditions the pilot reading on the microphone the same letters which he saw this time — at the same distance — through the barochamber visor. The movement of the letters on the kimograph band has simulated a situation similar to that of the sudden appearance and disappearance of images which might appear during high altitude flights in conditions of a somewhat similar estimation of speed and distances

We then followed systematically before and after the egress from the barochamber the dynamic visual accommodation of the clearest *punctum proximum* by measuring the distance between the retina and the nearest and most distinct visual point. For this purpose the aviator sitting on a chair with the back to the window, looked successively with each eye at the letter on an octotype for the near sight the letter being gradually brought nearer up to the limit at which its clear perception began to become slightly cloudy. For the commodity of the researches the proximeter conceived by M. Carapancea and M.

under the influence of the diminution of the oxygen in the blood, "markedly reduces — according to Mercier and Duguet(2) — accommodation amplitude." Along the same line, it was shown that after an hour's exposure in a plane, on a mountain, or in the broom-chamber, to a 5 000 m altitude, 10 minutes are necessary for the accommodation to return to normal(1). Altitude or spatial myopia has been noticed in numerous U S A pilots and observers, after 5-8 years of flight, hence the conclusion that emetropia does not ensure a permanent visual efficiency, but that only weak hypermetropia is a protection against this acquired myopia. The explanation of this professional myopia has been identified, according to Mercier and Robert(3), and Mercier(4), in the special state of accommodation induced by staring at a visual field completely devoid of details. In fact, it is well known that in the presence of an "empty" visual field, lacking all guide marks, relieved by perfect darkness, uniform fog, cloudless sky considered by clear atmosphere, as is the perfectly mat white screen of the high altitude sky, the eye is adapted for a *punctum remotum* corresponding to the "imagined" distance of 1-2 metres, with a special myopia of about 1 d.

In the case of the pilot, who should preferably be not an emetrope, but a hypermetrope, i.e. having a supernormal sight for great distances, the ciliary muscle is super stressed by the accommodation activity an effort continuously imposed for the far sight (even the sight to infinite — since *punctum remotum* is virtual and situated beyond the infinite) — as well as, and particularly for the near sight as *punctum proximum* — is placed at the back of the retina. Thus, the hypermetrope's sight is never distinct, whatever the distance to the object considered, except by a continuous accommodative effort, which ensures the stability of a clear sight. Thus, in the hypermetrope, the adaptation of the image, both for far sight, as well as for near sight, has the aspect of a continuously active phenomenon.

The number of accommodative acts, however, which are required of a pilot, is outright impressive. Platonov(5) writes: "Even on a training plane, with a speed of about 100 km an hour, for a single lap on the flight strip, from take off to landing, i.e. approximately 4 min the pilot is obliged to direct his attention 300 times from one object to another, in a strictly determined succession. In the much more complex jet plane, with the increased number of necessary reactions and the reduced available time the working rhythm becomes more rapid." Platonov(5) also shows that, if the pilot has a 1,5 visual acuity, he can identify an enemy plane which flies to meet him at the rate of 1 000 km per hour, from a distance of about 850 m. If he has however, a visual acuity of 0,5, he will only be able to make it at a smaller distance (about 115 metres). If we consider the speed of each plane as equal to only 270 km/hr (The approaching speed will be of 540 km/hr), then the pilot with a 1,5 visual acuity will have at his disposal, up to meeting moment, 5,5 sec., while the pilot with a 0,5 visual acuity will only dispose of 3,7 sec."

from the barochamber a much closer *punctum proximum* than the one observed before the hypopressure thus an increase in the amplitude of accommodative contraction. This nearing of the *punctum proximum* was usually directly proportional to the degree of the hypopressure at altitudes above 5 000 m. If on the ground the accommodative amplitude was comprised between 6 and 16 cm after the return from the flight it was between 5 and 14 cm at 5 000 m, between 5 and 13 at 12 000 m, between 5 and 12 at 15 000 m, between 5 and 10 at 16 000 m and between 4 and 8 cm at 18 000 m (Fig 2 3, 4, 5, 6)

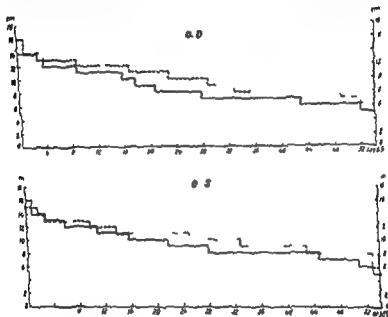


Fig 2

Punctum proximum on the ground (broken lines) and after hypobaric tests at 5 000 m (continuous lines) O.D. = right eye O.S. = left eye

We have also noticed that the *punctum proximum* is approaching much more in flight trained aviators and less in lesser trained ones much more in aviators trained at high altitudes than those trained at lesser altitudes

The duration of the maintenance of the close *punctum proximum* has varied between 5 and 15 min and was directly proportional to the degree of hypopressure in altitudes above 5 000 m to flight training and especially to training at high altitudes

3 Normal pupillary The pupillar diameter was rarely reduced by 0.5 mm as compared to the one previous to the barochamber altitude test

Popescu permitted by a method easily understood by the investigated person, the simple, rapid and precise determining of the *punctum proximum* (Fig 1)

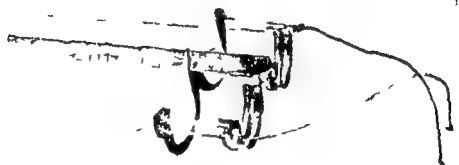


FIG 1

M Crayonceanu and M Popescu's PROXIMOMETER

At the same time, the behaviour of the irian muscle was also studied by iridokinesimetry or pupillometry, consisting in the comparative measurement of pupillar diameters before and after the barochamber tests

Researches were carried out on 51 visitors between 21 and 35 years of age, totaling, within the accommodation investigations a number of 2180 examinations in all the experimental variants described above while among investigations relating to pupillar modifications 382 examinations were carried out

## THE RESULT OF RESEARCHES

The researches carried out have yielded the following results

1 *Iachromatic and chromatic, static and dynamic visual accommodation of the punctum remotum* Before and after the altitude test, in the barochamber, this accommodation is normal while within the barochamber, at a hypopressure corresponding to altitudes of 5 000 and 12 000 m, in 21 out of the 51 visitors, the confusion of the colour of blue letters, perceived at 5/7 and 5/3 acuties, with that of black letters of the same dimension has been observed

2 *Dynamic, visual accommodation of a punctum proximum* Our proximometer has almost always emphasized immediately after the egress

hypopressure. The clearest *punctum proximum* determined with the proximeter is the more nearing the eyes the more the hypopressure corresponds to altitudes above 5 000 m and at the same time the more the aviator is trained in flight and especially in high altitude flights.

These facts suggest the following explanations

1 In conditions of barochamber hypopressure which induces the nearing of the *punctum proximum* a constant increase in the amplitude of crystalline refraction sets in subsequent to a proportional increase in the accommodative contraction of the ciliary muscle which is in a state of spasm. Under

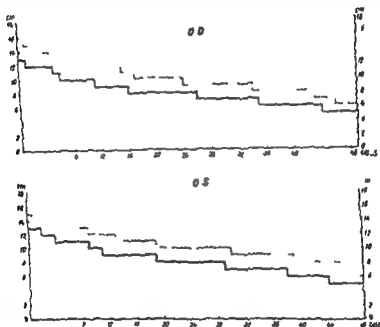


FIG. 4

*Punctum proximum* on the ground (broken lines) and after hypobaric tests at 15 000 m (continuous lines) OD — right eye OS — left eye

the influence of hypopressure and in proportion to it the ciliary muscle is fixed in a state of exaggerated accommodative contraction as against the one recorded previously on the ground where pressure was normal. The state of hypobarism accommodative contraction justifies the corresponding situation of the crystalline lens with a refringency of a myotic type which necessitates the perception of the *punctum proximum* at a smaller distance than that of the crystalline lens with normal refringency ordered by an uncontracted ciliary muscle in conditions of normal ground atmospheric pressure.



## INTERPRETATION OF RESULTS

The non coloured and coloured visual accommodation of the fixed and mobile *punctum remotum*, necessitating the adjusting of its image from the static and dynamic point of view, was normal before, during and after the barochamber altitude tests

We have, nevertheless, established in 21 out of the 54 aviators that in barochamber hypopressure, corresponding to the altitude of 5 000 m, the confusion of blue with black, for both subnormal (5/7) and hypernormal (5/3) visual acuities, has taken place

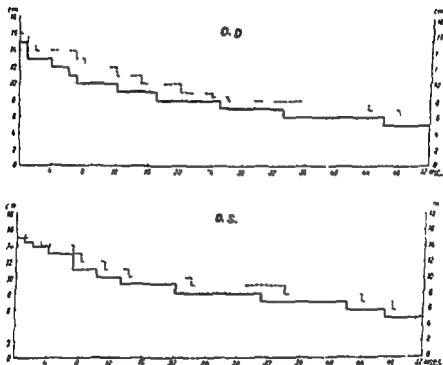


FIG. 3

Punctum proximum on the ground (broken lines) and after hypobaric tests at 12 000 m (continuous lines) O.D. = right eye O.S. = left eye

Our observation tallies with Platonov's (5) which shows that colour sensibility decreases slightly even at the slightest oxygen insufficiency, when the pilot begins to differentiate with difficulty certain colours and shades. It should be kept in mind that the decrease in colour sensibility begins sometimes even at the height of 2 000 to 5 000 m. Platonov (5) concludes: 'That is why in particularly important reconnaissance flights, oxygen should be used not as from 15,000 m but from a much lower altitude.'

Visual accommodation of a mobile *punctum proximum*, necessitating the adjustment of its dynamic image, evolving between the near and the nearest clear vision is plainly modified by high altitude

**hypopressure** The clearest *punctum proximum* determined with the proximeter, ■ the more nearing the eyes the more the hypopressure corresponds to altitudes above 5 000 m and at the same time the more the aviator is trained in flight and especially in high altitude flights

These facts suggest the following explanations

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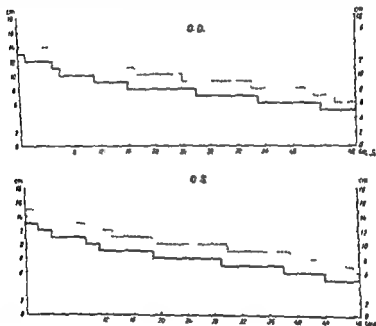


FIG 4

Punctum proximum on the ground (broken lines) and after hypobaric tests at 15 000 m (continuous lines) O D = right eye O S = left eye

the influence of hypopressure and in proportion to it the ciliary muscle is fixed in a state of exaggerated accommodative contraction as against the one recorded previously on the ground where pressure was normal The state of hypobarism accommodative contraction, justifies the corresponding situation of the crystalline lens with a refringency of a myotic type which necessitates the perception of the *punctum proximum* at a smaller distance than that of the crystalline lens with normal refringency ordered by an uncontracted ciliary muscle in conditions of normal ground atmospheric pressure

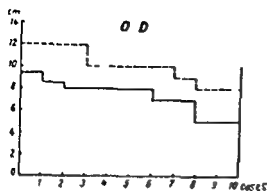


Fig. 5

Punctum proximum on the ground (broken lines) and after hypobaric tests at 16 000 m (continuous lines)  
O D - right eye O S - left eye

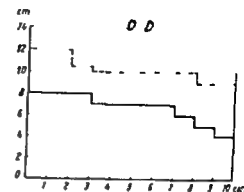


Fig. 6

Punctum proximum on the ground (broken lines) and after hypobaric tests at 18 000 m (continuous lines)  
O D - right eye O S - left eye

For this transient emetropia induced by hypobarism, we propose the name of *hypobaric myopia*.

At the beginning of the present paper we have stressed the present importance of the state of *anoxemic myopia* and *spatial or altitude myopia*, in the ocular physiology of the aviator.

We have, however, established, that in aviators, — in the impossibility of achieving spatial myopia — beginning by keeping him at a barochamber altitude of 5 000 m, without the inhalation of oxygen and then raising him to higher altitudes, when the inhalation of oxygen is compulsory, the accommodation contraction was *proportionally accentuated* with the altitude attained.

The following conclusion becomes evident if at 5 000 m hypoxemia acts together with hypobarism, at altitudes above 5 000 m, where hypoxemic action decreases, and that of hypobarism increases, this decreases predominantly the accommodation amplitude.

Thus — by the examination of the aviator, more subjected to hypopressure, decreasing the degree of anoxemia and eliminating the existence of any refractory *punctum remotum*, both possible generators of myopia — our researches disclose a new altitude emetropia the

altitude hypopressure myopia which sets in immediately and disappears shortly after the ceasing of the hypopressure action

2 Hypobaric myopia lasted between 5 and 15 minutes. Its duration was directly proportional to the degree of hypopressure of altitudes above 5 000 m, with flight training especially at high altitudes

The fact that the duration of hypopressure myopia is directly proportional to the degree of hypopressure above 5 000 m only underlines the greater intensity of the stability of ciliary spasm phenomenon under the influence of hypopressure

The fact that the duration of hypopressure myopia is directly proportional both to the flight training and to high altitude training, only underlines the adaptation promptitude of the ciliary muscle, probably hypertrophied in the meantime after the numerous solicitations of repeated hypopressures

In these conditions it seems beyond doubt that altitude hypobaric myopia is an important helping factor to the two myopias

There is apparently a contradiction in our experiences which show on the one hand that accommodation of the *punctum remotum* is realized normally while that of *punctum proximum* emphasizes a state of myopia

The contradiction is merely apparent

The distant sight is normal but the sight between *punctum remotum* and *punctum proximum* is that which is influenced by myopia set in by the influence of hypopressure. This altitude hypobaric myopia is all the more pronounced as the sight approaches *punctum proximum*

In this connection it is interesting to point out the fact of observation that the depth or stereoscopic acuity — connected with illumination precision of outlines and the distance of objects perceived binocularly as two slightly different retinal images — is according to Platonov (5) influenced in aviators by the insufficient oxygenation of the blood. Therefore after a high altitude flight it is recommended that before landing one or two tours of the landing strip be made (Platonov)

## PRACTICAL CONCLUSIONS

Disturbances of chromatic confusion of blue and black are only due to altitude hypoxia hence — as shown by Platonov (5) — the imperative necessity that in particularly important reconnaissance flights oxygen be used not from 4 500 m but from a much lower altitude

Altitude hypopressure myopia which we point out for the first time, — sets in immediately and disappears shortly after the action of hypopressure. It undoubtedly contributes considerably to the setting in of the state of altitude myopia by inducing a very near *punctum remotum* which in time becomes stable and irreversible

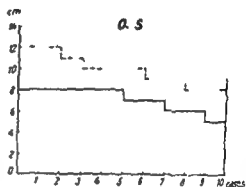
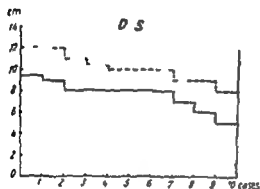
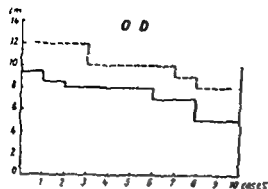


Fig 5

Fig 6

Punctum proximum on the ground (broken lines) and after hypobaric tests at 16 000 m (continuous lines)  
OD - right eye OS - left eye

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examination technique was based on the punctiform pressing of the hair, its curving thus achieving an elastic force which exercised a counter pressure which could be measured by the similar pressure on the dish of a balance. Von Frey's method required however hairs of different lengths, calibres and elasticities, depending on their age, a fact which constituted an important impediment for its clinical application. On the other hand the constancy of the hair's force varied in its turn with atmospheric humidity. These two serious inconveniences have impeded the spreading of von Frey's method.

Ingenious forms of apparatuses for determining these sensibilities have been conceived but in the course of time, they all have been proved inexact.

The current method of bulbar conjunctival and corneal sensibility investigation has, therefore, still remained the one which uses the touching of the eye with a finely twisted cotton wool pad in the form of a pointed brush. The touch (single stimulus) or the stroking (multiple and unequal stimuli) with cotton wool induces a more or less painful sensation in equal or more accentuated intensities in one part or another of the respective explored region as subjective phenomena and a blinking reflex as an objective phenomenon.

In 1952 in his thesis *About the Corneal Sensibility*, Jorn Boberg Ans (2) (3) has suggested a variant improving von Frey's method which consisted in replacing the hair by a nylon thread which has constant physical properties: is round and uniform. Thus the elasticity coefficient of the nylon thread with a 0,112 mm diameter and a length between 5 and 55 mm, achieves the series of pressures required for the measurement of corneal sensibility. Introduced into a special telescopic system this thread permits the variation in the length of the nylon thread. The author has computed the force ( $P_E$ ) which acts at the end of the elastic nylon thread by Euler's formula:

$$P_r = \frac{\pi^2 E I}{l^3}$$

In this formula  $l$  being the length of the thread

$I$  (inertia)  $= \frac{\pi^2 d^4}{64} = 0.049 d^4$  in which  $d$  (diameter of the thread) being 0,112 mm, the result is  $I = 0.72 \cdot 10^{-9} \text{ cm}^4$ .  $E$  (elasticity coefficient) in a nylon thread with  $L$  (length) and  $d$  (diameter) may be computed in variable conditions thus:

$$\text{with } 0\% \text{ relative humidity } E \text{ being } 4.92 \cdot 10^8 \quad P_L = \frac{710}{L^3} \text{ mg}$$

$$50\% \quad , \quad 3.16 \cdot 10^8 \quad P_E = \frac{450}{L^3} \text{ mg}$$

$$100\% \quad 1.19 \cdot 10^8 \quad P_E = \frac{170}{L^3} \text{ mg}$$

Hypobarism myopia is directly proportional to the degree of hypobarism, flight and high altitude training, which imply in the first case the intensity of the ciliary spasm, and in the other two,—according to the aviator's training—the prompt adaptation of the ciliary muscle, probably hypertrophied after the numerous solicitations of reiterated hypopressures.

It results in that the pilot who has become myope in conditions of high altitude flights cannot accommodate himself in normal conditions during the landing of present very rapid planes, when both the image of the ground which approaches very rapidly, and the image of the board apparatus, situated at fixed, constant distance, have to be adjusted.

The Laboratory for Clinical and Experimental Physiology and Physiopathology of the Eye of the Normal and Pathological Physiology Institute "Daniel Dănilopolu" of the Academy of the Romanian People's Republic. Director of the Institute Academician Prof. Dr. Gr. Bănescu.

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#### BULBAR CONJUNCTIVAL AND CORNEAL SENSIBILITY IN CONDITIONS OF HYPOBARISM IN HIGH ALTITUDE PILOTS

by

M. CARAPANCLA, M. POPESCU, L. RAIU, I. PINILIU  
M. SIOIAN and M. SILIAN  
(Roumania)

#### PREVIOUS RESEARCHES

The examination of the sensitivity of bulbar conjunctiva and cornea was previously carried out by touching them with a finely pointed bit of cotton wool.

In 1891, this inexact method had already been replaced by von Frey's, which employed hairs of various calibres and lengths. His



examination technique was based on the punctiform pressing of the hair, its curving thus achieving an elastic force which exercised a counter pressure which could be measured by the similar pressure on the dish of a balance. Von Frey's method required however hairs of different lengths, calibres and elasticities depending on their age, a fact which constituted an important impediment for its clinical application. On the other hand, the constancy of the hair's force varied in its turn with atmospheric humidity. These two serious inconveniences have impeded the spreading of von Frey's method.

Ingenuous forms of apparatuses for determining these sensibilities have been conceived but, in the course of time they all have been proved inexact.

The current method of bulbar conjunctival and corneal sensibility investigation has therefore still remained the one which uses the touching of the eye with a finely twisted cotton wool pad in the form of a pointed brush. The touch (single stimulus) or the stroking (multiple and unequal stimuli) with cotton wool, induces a more or less painful sensation in equal or more accentuated intensities in one part or another of the respective explored region as subjective phenomena and a blinking reflex as an objective phenomenon.

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$$P_2 = \frac{r^2 EI}{12}$$

In this formula  $l$  being the length of the thread

$I$  (inertia) =  $\frac{\pi^2 d^4}{64} = 0.049 d^4$  in which  $d$  (diameter of the thread) being 0.112 mm the result is  $I \approx 0.72 \times 10^{-9} \text{ cm}^4$   $E$  (elasticity coefficient) in a nylon thread with  $L$  (length) and  $d$  (diameter) may be computed in variable conditions thus

with  $0^\circ$  relative humidity E being  $4.92 \cdot 10^3$  P<sub>L</sub> =  $\frac{710}{1.1}$  mg

$$50\% \quad , \quad 3,16 \cdot 10^4 \text{ P.E.} = \frac{450}{14} \text{ mg}$$

$$100^\circ, \quad 1,19 \cdot 10^4, P_2 = \frac{170}{12} \text{ m}_g$$

In our country, Dr. Eugen Răutu and Eng. Anton Ivanovici have perfected the Boberg-Ans esthesiometer, by a guiding system of the thread inside the tube which contains it, thus averting the supplementary sliding of the nylon thread, as it happens in the Boberg-Ans apparatus.

In order to facilitate the reading of results, the authors have devised a table in which, in relation to the length in mm. of the nylon thread, its mg. pressure is shown, exercised according to the atmospheric humidity of the day in which the sensibility is examined, and since in Rumanian humidity varies between 50 and 80%, calculations were marked for every 10% humidity, and between 50 and 100%.

### OBJECT OF RESEARCHES

It is a known fact that young people present an average bulbar conjunctival sensibility of 72-200 mg., and an average corneal sensibility of 15 mg. or less in the center, and of 15-20 mg. in the sclero-corneal limbus. Corneal and conjunctival sensibilities decrease with age.

On the other hand, it is also known that intraocular pressure below 30 mm. Hg. (within limits considered as normal) does not determine any sensibility modification, while above 30 mm. Hg., the corneal sensibility threshold increases equivalently by 18-20 mg., up to 50-72 mg., whence it evidently results that corneal sensibility varies with intraocular pressure.

Our researches had in view to establish whether and to what extent, bulbar conjunctival and corneal sensibilities appear modified in conditions of the return from hypobarism, having in view the fact that, on the one hand, that this induces important disturbances in the arterial pressure of the cephalic segment, as was shown, both experimentally (1) and clinically (2), and therefore implicitly in the conjunctival sector, while, on the other hand, that ophthalmotonus decreases at high altitudes.

### RESEARCH TECHNIQUE

Our researches were carried out at the Aviation Medical Center during some of the tests which aviators are normally subjected to in view of the examination of their flight possibilities at different high altitudes. These tests consisted in the aviators being subjected in the bromochamber, to depressions corresponding to the altitudes of 5 000, 12 000, and 15 000 metres, the last two tests being carried out with administration of oxygen. Each of these three tests have been made on separate days, with two days rest between the tests.

In our examinations we have employed the esthesiometer conceived by the two Rumanian innovators.

Our investigations have only had in view the testing of the limiting sensibility threshold resulting from the slightest touch, and in verifying the reality of the perception of minimal sensation we made touch simulations.

We have avoided possible technical errors by holding the handle of the apparatus exactly over the point of contact applying the thread at right angles to the bulbar conjunctiva and the cornea, taking care that the thread curvature does not exceed 5% of its free length. The application of the point of the thread on the eye was made as slowly as possible so as always to have the same lightest and most constant excitation intensity, since the rapid application increases the effect of the stimulant.

We recorded for each eye separately the minimum perception of the bulbar conjunctiva and then of the cornea, by the examination always in the same succession, of the sensibility in the four cardinal points of the paralimbic bulbar conjunctiva at 3 mm from the sclero-corneal limbus (upper and nether by opening the palpebral slit with the thumb and the forefinger) and then by examining the sensibility always in the same succession in the four cardinal points of the paralimbic cornea and in the center of the cornea.

The bulbar conjunctival and corneal sensibility has been recorded in aviators in conditions of normal ground pressure before entering the barochamber and immediately after the egress from it, where they had been subjected to the above altitudes.

Our researches have been carried out on a lot of aviators of 21-35 years of age of whom not all had been subjected to all the tests. The esthesiometry of the bulbar conjunctiva and of the cornea have thus been examined in normal ground conditions in 45 cases while immediately after the return from the altitudes of 5 000, 12 000 and 15 000 metres respectively in 45, 43 and 39 cases.

The bi-ocular researches — effectuated in normal ground conditions and immediately after the return from the mentioned altitudes investigating the bulbar conjunctiva in four regions and the cornea in five regions — have totalized a number of 3 096 results the respective computation of which has been related to the Bucharest humidity during the period May 30 and June 23 1960 when this esthesiometry has been practised.

#### THE RESULT OF ESTHESIOMETRIC INVESTIGATIONS

Topographical esthesiograms of bulbar conjunctiva and cornea computed in mg pressure (Fig. 1) show the following results:

1. The esthesiogram of normal, ground bulbar conjunctiva is contained in O.D. (right eye) between 8 and 100 mg, the mean varying between 19.8 and 37.7 mg while the O.S. (left eye) between 12 and 100 mg the mean varying between 20.1 and 34.5 mg the threshold of this sensibility thus presenting a lower nether limit in O.D. than in O.S. (O.D. 8 mg, O.S. 12 mg) while the upper threshold limit is the same in A.O. (both eyes) (100 mg) in comparing topographical sensibilities it is also noticed that in A.O. the nasal region is the seat of the highest sensibility threshold of the entire

In our country, Dr Eugen Ratiu and Eng Anton Ivanovici have perfected the Boberg Ans esthesiometer, by a guiding system of the thread inside the tube which contains it, thus averting the supplementary sliding of the nylon thread, as it happens in the Boberg Ans apparatus.

In order to facilitate the reading of results, the authors have devised a table in which, in relation to the length in mm of the nylon thread, its mg pressure is shown, exercised according to the atmospheric humidity of the dry in which the sensibility is examined, and since in Rumania humidity varies between 50 and 80%, calculations were marked for every 10% humidity, and between 50 and 100%.

### OBJECT OF RESEARCHES

It is a known fact that young people present an average bulbar conjunctival sensibility of 72-200 mg, and in average corneal sensibility of 15 mg or less in the center, and of 15-20 mg in the sclero corneal limbus. Corneal and conjunctival sensibilities decrease with age.

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In our examinations we have employed the esthesiometer conceived by the two Rumanian innovators.

Our investigations have only had in view the testing of the liminary sensibility threshold resulting from the slightest touch, and in verifying the reality of the perception of minimal sensation we made touch simulations.

50 mg), comparing topographical sensibilities, it is also noticed that the higher and the lower region from O S have a threshold comprised between the same sensibility limits (12-84 mg).

4 Bulbar conjunctival esthesiogram recorded immediately after the return from the 15 000 m altitude, is comprised in O D between 18 and 450 mg the mean varying between 48.2 and 122.6 mg, while in O S between 16 and 450 mg, the mean varying between 44.7 and 117.8 mg; thus, this sensibility threshold presents a similar upper limit in A O (450 mg) while the neither threshold limit is higher in O D than in O S (O D 18 mg O S 16 mg), comparing the topographic sensibilities it is also noticed that the temporal region of A O is the seat of the highest sensibility threshold of the entire bulbar conjunctival surface (450 mg) equally the temporal and nasal regions have similar sensibility thresholds (temporal A O 26-450 mg nasal A O 33-320 mg) while the higher and lower regions from O D, have a threshold contained within the same sensibility limits (18-112 mg). The corneal esthesiogram also recorded immediately after the return from the 15 000 m altitude is contained in A O between 15 and 84 mg the mean varying in O D between 29.2 and 33 mg while in O S between 29.3 and 35.7 mg, thus, this sensibility threshold presents in A O a both higher and lower limit identity comparing topographical sensibilities, it is noticed that the regions temporal from O D and the neither from O S are the seat of a threshold contained within the same sensibility limits (15-50 mg) and that the A O nasal regions have likewise a sensibility threshold contained within the same limits (16-84 mg).

The general mean of A O topographic esthesiograms (Fig 1) shows both in bulbar conjunctiva and in cornea a directly proportional rise in the mean sensibility threshold of all investigated regions.

The systematic rise in the extreme neither and upper limits of the sensibility threshold takes place up to 15 000 m where as compared to thresholds recorded at 12 000 m, we find that if the lower conjunctival region presents a lowered neither limit and a stationary upper limit the higher lower and temporal corneal regions present a lowered upper limit.

The resulting general mean of the bulbar conjunctival and corneal global sensibilities computed in mg pressures (Fig 2) shows a rise in both sensibility thresholds, in proportion to the altitude from which it returned but more rapid and marked in bulbar conjunctiva than in cornea.

Mean global sensibilities of bulbar conjunctiva and cornea reckoned in mg pressure, in 39 cases distributed in three category groups identical in both eyes starting from the bulbar conjunctival sensibility recorded as from 15 000 m to the ground (Fig 3a, b) point out to the following facts.

The thresholds of both ocular sensibilities exhibit — within their rises proportional to the altitude from which they return, but more

bulbar conjunctival surface (100 mg) Normal, ground corneal esthesiogram is contained in O D between 8 and 28 mg, the mean varying between 12,5 and 13,1 mg, while in O S between 8 and 23 mg, with a mean varying between 12,5 and 13,2 mg, so that this sensibility threshold presents a higher upper limit in O D, than in O S (O D 28 mg, O S 23 mg), while the nether threshold limit is the same in A O (8 mg), comparing topographic sensibilities, it is also noticed, on the one hand, that the central region threshold is identical in A O, and, on the other hand, that in each eye the temporal and nasal regions, and the higher and lower ones have a threshold contained between the same sensibility limits (temporal and nasal O D 8-28 mg, higher and lower O D 8-23 mg, temporal and nasal O S 8-23 mg, higher and lower O S 8-19 mg)

2 Bulbar conjunctival esthesiogram, recorded immediately after the return from the altitude of 5 000 m, is contained in A O between 12 and 182 mg, the mean varying in O D between 29,7 and 7,31 mg, while in O S between 32,1 and 68,9 mg, so that this sensibility threshold presents in A O a limit identity, both higher and lower, comparing the topographic sensibilities, it is also noticed that in A O the nasal region is the seat of the highest sensibility threshold of the entire bulbar conjunctival surface (182 mg) The corneal esthesiogram also recorded immediately after the return from the 5 000 m altitude, is contained in O D between 8 and 50 mg, with the mean varying between 21,4 and 22,9 mg, while in O S between 9 and 50 mg, with the mean varying between 21,9 and 22,4 mg, thus the sensibility threshold presents a nether limit, slightly higher in O S than in O D (O S 9 mg, O D 8 mg), while the upper threshold limit is the same in A O (50 mg), comparing topographic sensibilities it is also noticed that in O S the temporal and nasal regions have a threshold contained between the same sensibility limits (9-42 mg)

3 Bulbar conjunctival esthesiogram recorded immediately on return from the 12 000 m altitude, is contained in O D between 18 and 182 mg, the mean varying between 41,9 and 87,3 mg, while in O S between 15 and 320 mg, the mean varying between 38,4 and 87,1 mg, this sensibility threshold thus presenting a higher upper limit in O S than in O D (O S 320 mg, O D 182 mg), and a higher nether limit in O D than in O S (O D 18 mg, O S 15 mg) comparing topographic sensibilities, it is also noticed that in the A O nasal region is the seat of the highest sensibility threshold of the entire bulbar conjunctival surface (O S 320 mg O D 182 mg), while the O D higher and lower regions have a threshold contained between the same sensibility regions (18-100 mg) The corneal esthesiogram also recorded immediately after the return from the 12 000 m altitude is comprised between 12 and 50 mg, the mean varying between 25,5 and 27,6 mg, while in the O S between 12 and 84 mg the mean varying between 27,9 and 31,4 mg, this sensibility threshold thus presenting a similar nether limit in A O (12 mg), while the upper threshold limit is higher in O S than in O D (O S 84 mg, O D



## THERAPY

The treatment of Eales's disease has been unsatisfactory. Various therapeutic measures like iodides, thyroid, oestrogens, vitamin C, vitamin B and vitamin P have been used in the past but without any benefit. Results with antitubercular drugs have been disappointing. Belz and Bouche (1951)<sup>(25)</sup> recommended ultrasonics to disperse the blood clots but the fate of this therapy has in no way been better than those preceding it. Guyton and Reese (1948)<sup>(26)</sup> and many others have claimed good results by X-ray and radiation therapy but Merriam (1956)<sup>(27)</sup> found irradiation to be of hardly any help. Elliot (1954 and 1957)<sup>(28 & 29)</sup> claimed good results with continuous subconjunctival hydrocortisone therapy. We subjected our cases of Eales's disease to varied forms of therapy and divided them into four groups (Table III).

A 25 mgms of subconjunctival hydrocortisone every two weeks — 16 cases

B 25 mgm subconjunctival hydrocortisone every two weeks and 25 mgm androgen 1 m twice a week — 9 cases

C 25 mgm subconjunctival hydrocortisone every two weeks and choline and methionine on alternate days — 12 cases

D A combined therapy of 25 mgm of subconjunctival hydrocortisone every 2 weeks, 25 mgm of androgen intramuscularly twice a week and of choline and methionine on alternate days — 21 cases

The treatment was carried out for a period of 6 months to one year in every case and have been under observation for a period of 2 years or more.

Our results show that in group A 4 out of the 16 cases treated showed a recurrence. The series is comparable to the series of Elliot (1954)<sup>(28, 29)</sup> and Agarwal et al (in press).

In group B there were recurrences in 2 out of the 9 cases treated and the results are almost the same as in group A. Androgens do not seem to influence the results. In group C there were recurrences in 2 out of the 12 cases treated and the results are superior to those of groups B and A. The therapy in group C was instituted because of the positive history of liver disease in several of our cases and the knowledge that experimental choline deficiency can lead to retinal haemorrhages. Even in tubercular haemorrhagic lesions of the retina choline has shown beneficial results due to its lipotropic and anti haemorrhagic action.<sup>(30)</sup>

In group D there were recurrences in 2 out of 21 cases. This group includes cases which had been previously treated either in group A or B or C and had shown the recurrence of the disease also. From these results the combined therapy seems to be quite useful.

Diathermic closure of bleeding vessels in perivasculitis has been put to practice with encouraging results.<sup>(31, 32)</sup>

Light coagulation<sup>(31)</sup> is now being utilised for the same purpose. In twelve cases we utilised transcleral diathermy coagulation but



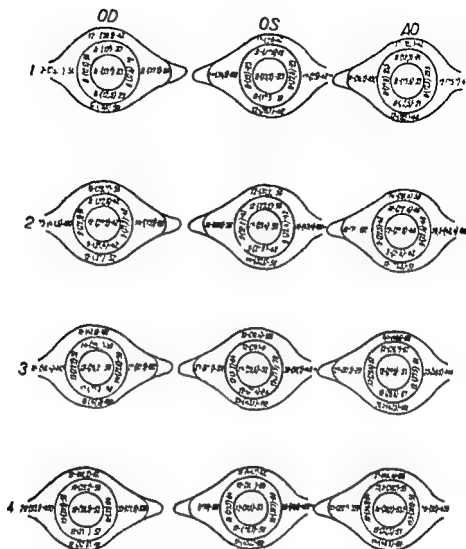


FIG. 1

Mean topographic esthesiograms of bulbar conjunctiva and cornea in mgr pressure in the right eye (O D) in the left eye (O S) with their general resultant in both eyes (A O) normal on the ground (1) and immediately after the return from the 5 000 m (2) 12 000 m (3) and 10 000 m (4) altitudes

rapid and marked in bulbar conjunctiva than in cornea — a parallelism evidently between groups, both within the sensibility of the same eye as between the right and the left eye

#### INTERPRETATION OF RESULTS

In our country, these two ocular sensibilities normally present the following characteristics

1 Bulbar conjunctival sensibility is comprised between 11 and 100 mg, the mean varying between 19,9 and 36,1 mg, and presents the sort of both thresholds in the nasal region

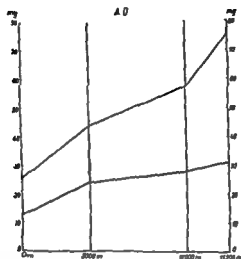


FIG 2

The resultant general mean of global sensitivities of bulbar conjunctiva (above) and of cornea (below) in mmgr pressure in both eyes (A O) normal on the ground and immediately after the return from the 5 000 m, 12 000 m and 15 000 m altitudes

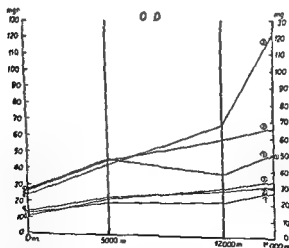


FIG 3a

Mean global sensitivities of bulbar conjunctiva (above) and of cornea (Fig 3b) in mmgr pressure in the right eye (O D) and in the left eye (O S) normal on the ground and immediately after the return from the 5 000 m, 12 000 m and 15 000 m altitudes in three identical category groups for both eyes (1) (2) (3) as against the same altitudes

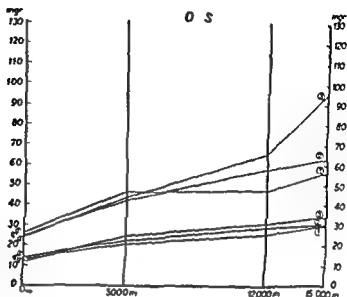


Fig. 3b

2 The corneal sensibility is comprised between 8 and 25,5 mg, the mean varying between 12,3 and 12,8 mg, and presents the seat of the nether threshold, identical on the entire surface of the cornea, and the seat of the upper threshold, identical in the nasal and temporal regions

Hence it results that the bulbar conjunctival sensibility has its extreme thresholds concentrated only in the nasal region, while the corneal sensibility has its nether threshold diffused on the entire surface of the cornea, and the upper threshold in the nasal and temporal regions, where it is identical

At altitudes of 5 000, 12 000 and 15 000 mm the extreme thresholds of both ocular sensibilities move their topographic seat in an orderless succession. Thus it results that the local innervation factor — which could explain on the ground the topographic seat of thresholds — can now no longer justify the changed seat of sensibility thresholds, and that the appearance of a threshold in another region than in the one in which it existed on the ground or at the previous altitude, points out to the removal of previous sensibility limits at the setting up of a new state of sensibility.

But, if the topographical thresholds of each ocular sensibility become partially modified, both sensibilities — considered in their general mean, a resultant of global sensibilities — return unmodified the normal ground, threshold relation of the general sensibility of bulbar conjunctiva, very much higher, as against that of the cornea. They manifest an ascent proportional to the altitude from which they return, but more rapid and marked in bulbar conjunctiva than in cornea. The threshold ascent of ocular sensibilities is manifest both for all cases in general, in both eyes taken together, and particularly for groups of cases, either in each eye considered separately or in comparison with the opposite eye, when an almost perfect concordance of sensibilities is noticed.

Thus the altitude raises proportionally with its own level, the tactile sensation threshold of the two anatomic functional individualities of the ocular anterior hemisphere but within each individuality the tactile sensation modifies in a disorderly way its topographic distribution.

### CONCLUSIONS — THERAPEUTICAL SUGGESTIONS

The disorderly modifications of topographic thresholds within each of the two ocular sensibilities are due in the bulbar conjunctiva to vascular disturbances which occur in the arterial pressure of the cephalic segment and implicitly in the conjunctive region while in the cornea they are the consequence of the ophthalmotonus returned now to normal after it had previously decreased at high altitudes.

The normal relation from the ground between the much higher general sensibility threshold of the bulbar conjunctive, as against the cornea, is being maintained and accentuated with the increased distance between them in proportion to the altitude from which they returned particularly because of the more rapid and marked ascent of the bulbar conjunctival threshold.

This reduced sensibility comparable to the nervous lesion of a transitory anaesthetic type and with a *reduced trobhesy* significance constitutes a favourable biological fund for any lesion infection or any other eventual pathological process the healing of which will be achieved slower if the pathological process sets in either immediately after landing or especially during the flight. Hence the necessity that both in engaging and at the periodical controls of aviators both sensibilities be normal. In any case it should be compulsory that before any conjunctival or corneal treatment an esthesiometrical examination of the aviator be carried out in order to investigate and have also in view the functional state of the subject under treatment.

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# OCULAR MANIFESTATIONS OF THE MECHANISM OF THE ACTION OF STRYCHNINE ON THE ORGANISM SET IN CONDITIONS OF HYPOBARISM AT HIGH ALTITUDES

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Previous, recent researches, both clinical, carried out at the Aviation Medical Center (7)(8)(9), and experimental, executed at our Institute (6), have shown that the eye constitutes a delicate indicator of modifications appearing in the functional equilibrium of the organism subjected to the action of high altitude hypobarism.

Experimental researches (6) have emphasized the following principal modifications: 1 *Mydriasis*, as a consequence both of the CO<sub>2</sub> accumulation, which excites the higher nervous centers (as evidence the fact that the pupil immediately reverts to normal if the barochamber is being ventilated, the atmospheric pressure being maintained unchanged), as well as of the algo-irido motor reflex, induced by the painful mechanical excitation of the respective intero-receptors, by the increased volume of gases which distend the viscera and the myelinic cover of the sensitive nerves, in proportion to the depression (as evidence the pupil reverting to normal, together with the re-establishing of atmospheric pressure). The third, mydriatogenous mechanism is, undoubtedly, connected with the *anxious* hyperadrenalinemia described by Malmgren and Chardon (12), who have shown, on the one hand that *anoxymia* induces the hyperactivity of the medullo-suprarenal gland and the increase in adrenaline secretion, and on the other, the fact that the severing of the splanchnic nerves — i.e. the denervation of the suprarenal glands — stops the *anxious* hyperadrenalinemia, along the same line we may mention that Prof. I. I. Nănescu has noticed the increased weight of the suprarenal capsules of the animal, after its being subjected to hypobarism. In the state of maximum 9 mm mydriasis, which occurs at a 200 mm Hg depression, the photo-irido motor reflex no longer appears, but it only occurs after a prolonged luminous excitation, in a medium 7 mm mydriasis, which had appeared at the 100–300 mm Hg depression, a fact which indicates the proportionally swiftly differentiated rise in the threshold of this reflex alongside the atmospheric pressure. 2 *The rapid chorio-retinal arteriolar spasm, followed immediately by the established chorio-retinal arteriolar dilatation accompanied by the respective venolar dilatation* — the vascular spasm is the consequence of the suddenly and abnormally increased blood flow under the influence of hypoxia, indicating a vascular defence reflex reaction, while the visodilatation is the consequence of hypoxia itself — proof that, if the same altitude is maintained, it disappears on the ventilation of the barochamber — indicating a vascular decompensation phenomenon. 3 *The diffuse retinal oedema in relatively circular zones, situated near the papilla*, is the

consequence of the derangement of certain endocular bio physico chemical mechanisms which locally modifying the normal osmotic exchanges, have induced the call of fluid into the retina, which in time, may constitute the starting point for an eventual detachment of the retina 4 *The aero embolism of the branches of the retinal vascular tree, and sometimes the orbital aero embolism* the former is the consequence of the liberation of gases dissolved in tissues in the form of gaseous bubbles dragged along by the circulatory stream, while the second is the consequence of the freeing of gases dissolved in the retroocular adipose tissue, in the form of diffu ■ gaseous infiltration of the orbital cellular tissue — orbital emphysema — with the consecutive protrusion of the eye and the sensation of crepitation at a slight pressure of the eyeball in the orbit

Knowing the behaviour of certain ocular components in connection with the general behaviour of the rabbit our research animal set in conditions of high altitude hypobarism we intended to establish whether and to what extent the same research animal set in similar experimental conditions but influenced by strychnine a drug with a central excitant action, studied by some of us in previous complex researches (1)(2)(3)(4), exhibits this time improved or aggravated general or ocular behaviours In the latter case, Cluzet, Piery, Ponthus, Mithaud (10) have shown that strychnine has often enabled animals to resist better to strong depressions and to attenuate or delay electro cardiogramic modifications

Establishing the behaviour of the animal in these combined experimental conditions is of use in the first place for determining the mechanism of the action of strychnine in conditions of high altitude hypobarism and still more so for the eventual therapeutical suggestions which may offer valuable indications for aviation medicine

## RESEARCH METHOD

The research was first carried out on the ground and then in the barochamber in order to appreciate correctly by comparison, the ocular manifestations of the organism strychninized and set in conditions of high altitude hypobarism as against ocular manifestations of the strychninized organism in conditions of normal atmospheric pressure

### 1 *The strychninization in conditions of normal atmospheric pressure*

The action of strychnine on the research animal (rabbit) has been performed (1) by direct (local) ocular and indirect (general) ocular contact

*The direct (local) ocular contact* has been practised either (though seldom) by *subconjunctival injections* or (almost always) by *mono or bilateral instillations* both on eyeballs with normal permeable, lachrymal ducts (permitting lachrymal draining by the normal ducts into the higher digestive duct) or rendered experimentally impervious (by the cauterization of palpebral lachrymal points 5 days before the



instillation, in order that, at the moment of the experiment, the painful mydriatic factor should have disappeared and the cicatrization finished, the variable factor of the lachrymal dilution has always been avoided by the absorption with filter paper of the tears present at the beginning of the experiment, which was carried out without immobilizing the animal or its head, and with the utmost gentleness by soaking the filter paper in the lachrymal fluid at the bottom of the lower conjunctival *fornix conjunctivae*, rendered evident by the delicate traction downwards, by the thumb, of the lower lid, without touching the corner or the conjunctiva, in other words, the tears were removed without fear or pain — both engendering mydriasis — for the animal.

*The indirect (general) contact has been practised either, though rarely, by intravenous injections or, almost always by subdural mono or bilateral injections or by mono- or bilateral cortical application of filter paper washers or cotton wool pads imbibed with strychnine*

Researches were carried out both separately with each experimental type or by the consecutive and synchronous interference of all these, as for instance strychnine has been put in contact with the organism, simultaneously or at different times, either by its monocular instillation associated with its monocular cortical application on the opposite or on the same side of the instillation, or by its biocular instillation with its cortical mono- or bilateral application, etc

We have thus studied the action of strychnine upon the tonicity of periocular, *musculus* and corio-retinal vascular musculature in albino rabbits

*The study of the dynamics of periocular musculature has been carried out by the observation of the movements of the eyeball*

*The study of the dynamics of the musculature of the iris — has been executed by measuring the pupillary diameter after the contact of the organism with the respective drugs. Dynamic pupillometry, i.e. the measurements of the movements of the apparent pupillar diameter — the real one being modified by the increased diopter corner — aqueous humour — indicates in substance, objectively the irido kinesimetry, i.e. the measurement of the dynamics of the musculature of the iris. Irido kinesimetry has been performed as follows in the animal placed on the observation table, always identically illuminated, with its eyes exposed to an invariable source of light, situated medially at the extremity of its nose and from below upwards, the pupillary diameter was measured with a metallic blade, millimetrically graduated, superposed parallelly to the pupillary plane, and as near as possible to the eye. As the rabbit eye is oval, with a vertical great axis, we have always measured, for commodity sake, its horizontal diameter*

In our researches we have tried to eliminate all factors of error which may modify the pupil, due to causes foreign to those of the action of the drug studied. To this effect we have removed from the beginning the two factors of error — pain and fear — each partially inducing mydriasis, to this effect, after being taken out of its hutch,

the rabbit was not only not incommodated by any immobilization, but was left to calm down for 30 minutes on the observation table and for subsequent experimental necessities the animal was handled with the utmost calm and kindness. The experiment was always carried out only on rabbits with normal pupillar diameters i.e. rigorously bilaterally exact in their horizontal diameter slightly inconstant variable around 5 mm and which reduced itself to 4 mm by the photo indo motor myosis incited by the 5 V Zeiss ophthalmoscope.

*The study of the dynamics of the musculature of corio retinal vessels in albino rabbits* was carried out by ophthalmoscopic examination of the modifications of the vascular calibre.

## 2 *The strychninization in conditions of high altitude hypobarism*

In some of the tests the rabbit was left free in the barochamber in order to observe its general behaviour as well as, at the same time and within possibilities the ocular one in general. In other tests the rabbit was immobilized without fastening its head for the bilateral observation within possibilities of the movements of the eyeball and of the pupillar and corio retinal modifications. In the third group of tests the rabbit was immobilized with the head fastened in flexion to the right or left resting on the transparent window of the barochamber for observing the movements of the eyeball and measuring the modifications in the pupillary diameter, as well as to explore ophthalmoscopically the blood vessels in the eye fundus.

The rabbit was then submitted with or without strychninization to very high ascents between 8 000 and 12 000 m corresponding to atmospheric pressures between 267 and 145 mm Hg. The ascent to 8 000 m took 1 min 50 sec, and the return to the ground 37 sec; the ascent to 9 000 m 2 min 5 sec and the return 40 sec; the ascent to 10 000 m 2 min 24 sec, and the return 44 sec; the ascent to 11 000 m 2 min 40 sec and the return 48 sec; and the ascent to 12 000 m 2 min 58 sec and the return to the ground 53 sec.

The experimental prototype most often used has been the ascent to 9 000 m i.e. to 230 mm Hg atmospheric pressure with a 3 min exposure and a subsequent 3 min rest on the ground. At one sitting the same animal was subjected up to ten ascents and in a period of one to three days in another 2-3 sittings to a total of 23 ascents.

All strychninization techniques used on the ground achieving the same general and ocular effect — as seen below — the strychninization used during the fictitious ascents in the barochamber consisted in the direct ocular (local) contact of mono and bilateral strychnine instillations on the eyeballs with normal permeable lachrymal ducts.

*The study of the dynamics of musculatures per ocular of the iris and of the chorio retinal blood vessels in albino rabbits* has been carried out in conditions of investigation similar to those performed with strychnine on the ground. We mention that the study of the dynamics of the musculature of the iris has been carried out in constant luminous conditions by

measuring the pupillary diameter with a metallic blade, millimetrically graduated, pressed to the window of the barochamber and superposed parallelly to the horizontal pupillary plane. The pupillary modifications, determined by the action of strychnine upon the rabbit in conditions of high altitude barochamber, have also been studied in connection with the photo-motor reflex.

## THE RESULT OF THE RESEARCHES

### 1° *Strychninization in conditions of normal atmospheric pressure*

*1st Experiment* 0,05-0,10 ml monocular subconjunctival injection or monocular instillation of 1-2 drops, both in 1% strychnine solution, induce after 1-6 min generalized tonic or tonico clonic convulsions, accompanied by disorderly and transient nystagmiformous jerks, intensive and generalized retinal arteriolar spasms and bilateral maximum mydriasis, which are usually followed by a state of sleepiness concomitantly with the disappearance of the phenomena described and the setting up of myosis, or often exitus. N.B. the effect is more delayed in the case of instillations on the eyeball with experimentally impermeabilized lachrymal ducts, than on the eyeball with normal permeable lachrymal ducts.

*2nd Experiment* The intravenous injection, the subdural, mono or bilateral injection, both of 0,05-0,10 ml of a 1% strychnine solution, the cortical mono or bilateral application of filter paper washer or cotton wool wads, impregnated with a 1% strychnine solution, induce, after a few seconds, the same phenomena, followed almost always by exitus.

*3rd Experiment* Ocular instillation or cortical application of a 1% strychnine solution to animals with the cortex previously brought into contact with a 10% chloral hydrate, have no effect or may induce, though very belatedly and very reducedly, the general and ocular phenomena described above, mydriasis may be replaced by sleep myosis.

### 2° *Strychninization in conditions of high altitude hypobarism*

Researches carried out in conditions of fictitious high altitude hypobarism in barochamber, without and with the mono and bilateral instillation of 1-2 drops of a 1% strychnine solution (for comparison purposes) yielded the following results.

1 The general resistance of the animal decreases proportionally, on the one hand, to the ascent to heights of between 8 000 and 12 000 m, and, on the other, to the time of exposure at these heights. Thus, dyspnea, rhythmic pulsation of the head, cyanosis of the mucous membrane of the nose, abdominal distension, mydriasis, chorio retinal vasodilatation set in ever clearer and more rapidly, the higher the ascent and the longer its action lasts, finally reaching exitus.

in seven of these 12 cases there was recurrence and another vein in a different quadrant was found to be involved. My learned colleagues to follow will throw more light on this problem.

The aetiology of Eales's disease still eludes us and the therapy remains empirical and conjectural. A combined therapy of hydrocortisone and methuine and choline does hold promise and is worthy of a trial. The prognosis of the condition has shown some improvement during recent years but still remains gloomy.

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2 The general resistance of the animal increases by the repetition in time of ascents—i.e. with training—and less by the time of exposure in these ascents. The known phenomena present, this time, a delayed appearance and an attenuated manifestation.

3 The general resistance of the animal is variably modified by previous strychnine instillations. Thus, after the ascents supported with difficulty the strychnine instillations, in a small dose increases to such an extent the resistance of the untrained animal and all the more so that of the trained one that it can easily be ascended anew, but this time to a higher altitude than the one before, while the return to normal during the rest, at atmospheric pressure on the ground, occurs evidently more rapidly. The high excitability threshold of the animal—contained between the upper limit, where no apparent effect is manifest and the lower limit reached sometimes and rendered evident by a slight mydriasis together with the state of slight general tremblings, occurring after slapping the animal slightly on the back with the palm—accompanies the increased resistance of the organism to ascents. The strychnine instillation in a large dose inducing tonic and tonico-clonic convulsions reduces the resistance of organism, both in trained and untrained animals even in connection with ascents which were easily supported before strychninization while the return to normal during the rest on the ground is much delayed or replaced by exitus. The very reduced excitability threshold of the animal—contained between the upper limit where generalized convulsions disorderly and transient nystagmiformous jerks generalized retinal arteriolar spasms and intensive maximum bilateral mydriasis, that appear together in similar intensities and the lower limit reached by exitus—accompany the reduced resistance by the organism in ascents.

The photo-motor reflex is absent during the maximum mydriasis it is much delayed during medium mydriasis and only slightly delayed in the case of discreet mydriasis.

#### INTERPRETATION OF RESEARCHES

##### 1 Strychninization in conditions of normal atmospheric pressure

It is therefore evident that the action of strychnine brought into contact directly ocularly or centrally manifests itself in both cases in the same manner as after the contact of strychnine with the cortex, by the intermediary of the same natural, chemical mediator, liberated subsequently and with a multiple effect upon the eye (1).

Instilled into the fornix conjunctivae of the O.S., the strychnine is being resorbed either slowly only through the conjunctive if the experimental obstruction of the lachrymal ducts has been induced or rapidly by the normal lachrymal ducts, oesophagus and stomach. The resorbed strychnine passes in both cases into the sanguine circuit and reaches the higher nervous centres. The slow resorption takes place by the higher conjunctivo-angio-nervous way, while the rapid resorption by the higher lachrymo-nasal digestive angio-nervous

way. Whether the strychnine reaches, by these ways with an ocular starting point, the higher nervous centres, or is set directly into contact with these centres, it increases their reactivity towards the Ach, which stimulates the centres and induces, on the one hand, tonic or tonico clonic convulsions and disorderly and transient nystagmiciform jerks, by the neuro muscular way, while, on the other hand, it stimulates the suprarenal capsule by the neuro suprarenal way. Adrenaline actively freed and disseminated throughout the organism by the sanguine way, influences the heart with the vessels of the general circulation, among which also the ocular vascular tree, determining general and intensive arteriolar spasms, visible ophthalmoscopically, and maximum bilateral mydriasis by the suprarenal angio retino irino way.

The histamine, produced in consequence of the increased exertion of the musculature submitted to alternations of muscular contractions and decontractions, manifested in the form of generalized convulsions, and in consequence of the increased work of the organs in general, impedes the higher nervous centres and leads to the state of torpor, which constitutes the state of histaminic shock, in the course of which the myosis also manifests itself.

An evidence that strychnine raises the reactivity of the higher nervous centres towards the Ach, which stimulates the centres and then unleashes the respective mechanisms and phenomena, is the fact that the chloral hydrate in a large dose with the "impeding action upon the nervous system towards the Ach", after Danielopolu (11) suppresses or at least admits a very tardy and reduced manifestation of the general and ocular phenomena which strychnine alone induces immediately and exaggeratedly.

## *2° The strychnization in conditions of high altitude hypobarism*

The general resistance of the untrained and trained animal is evidently increased by strychnine instillations in a small dose which is non convulsive, while, evidently, the general resistance is reduced by strychnine instillations in a large dose, which is convulsive.

In the first case we have a stimulation of the organism, while in the second an exhaustion of the organism leading to exitus.

Thus the action of strychnine depends upon the dose administered.

The ocular manifestations within the mechanism of the action of strychnine upon the animal set in conditions of high altitude hypobarism show, themselves, the degree by which strychnine increases the reactivity of the higher nervous centres towards the Ach, which stimulates the centres in the respective intensity, determining, on the one hand, in a small dose the rise in the general excitability threshold, contained between the higher level, where no phenomenon is apparent, and the lower limit, where a discreet mydriasis and a state of generalized slight tremblings set in, at the light tapping with the palm, on the back of the animal, and inducing, on the other hand, in a large

dose a very accentuated lowering of the general excitability threshold, contained between the higher limit, exhibiting the following phenomena which occur together in similar intensities tonic and tonico clonic convulsions with disorderly and transient nystagmiformous jerks generalized and intensive retinal arteriolar spasms and maximum bilateral mydriasis and the lower limit reached by exitus

Thus in a small dose strychnine raises slightly the reactivity of the higher nervous centres towards the Ach which stimulates these centres in the same degree and sometimes determines manifestations which indicate the reaching of the lower limit of the raised general excitability threshold. In this case the stimulation of the higher nervous centres by the Ach in consequence of the increase in the reactivity of the centres towards the Ach under the influence of the small dose of strychnine induces by the three following ways the manifestations described above namely by the *neuro muscular way* the state of delicate generalized tremblings at the slight superadded excitation of a light tapping with the palm on the back of the animal by the *neuro suprarenal way* the slight stimulation of the suprarenal capsule by the *suprarenal angio-irritant way* the discreet state of bilateral adrenalinic mydriasis by the slight increase in the irido dilatating tonus and the slight decrease in the irido constrictor tonus

In a large dose however strychnine raises exaggeratedly the reactivity of the higher nervous centres towards the Ach which stimulates similarly these centres and induces phenomena which indicate the very marked decrease in the general excitability threshold. In this case the stimulation of the higher nervous centres by Ach in consequence of the increase in the reactivity of these centres towards the Ach under the influence of the large dose of strychnine, induces by the following three ways the above described manifestations namely by the *neuro muscular way* the state of tonic and tonico clonic convulsions accompanied by disorderly and transient nystagmiformous jerks by the *neuro suprarenal way* the strong excitation of the suprarenal capsule by the *suprarenal angio-irritant way* generalized and intensive retinal arteriolar spasms accompanied by maximum bilateral adrenalinic mydriasis following the great increase in the irido dilatating tonus and the great decrease in the irido constrictor tonus

In a small dose therefore with a weak action strychnine yields similar effects to those of any other central stimulant of any nature (psychic physical chemical) but with the same slight intensity of action which raises the general excitability threshold between a higher limit, where there is no apparent phenomenon and a lower limit where a discreet mydriasis and eventually a light state of general hyperexcitability set in

In this respect in the researches of some of us (5) it was shown for instance that in the case of glaucoma in which a psychic factor is acting and thus with a central action this increases slightly the reactivity of the higher nervous centres towards the Ach which stimulates slightly the higher nervous centre and stimulate most discreetly

the suprarenal capsule, while the actively liberated adrenaline in a very small quantity and spread throughout the organism by the sanguine way, accompanied by a local ocular factor, with a propensity to glaucoma, determines the glaucomatous mydriasis.

The fact that the adrenaline enters the physiopathological circuit of the glaucoma has been demonstrated by Popov (quoted at (13)) who, analysing the blood of the glaucomatous patients, has discovered in most of them an increase in Cr and Atr, accompanied by a decrease in K, I and choline. In the same sense, Pluinev, Raeva and Voronina (quoted at (13))—examining, by the Levi method, the aqueous humour of glaucomatous persons, have brought to light the presence of the adrenalinic sympathotrophic chemical mediator, which raises the activity of the heart and much more seldom that of the vagotrophic substance, the acetylcholine, which diminishes the activity of the heart, a proof of the disturbance of the sympathetic-parasympathetic equilibrium of the nervous vegetative system in the glaucoma, with a sympathetic predominance.

These facts constitute yet another argument in favour of mydriatogenous adrenalinic mechanism, generally a consequence of any central excitant, their different action intensities explain the degree of the mydriatic manifestation, in the sense that the discreet mydriasis is the consequence of any weak central excitant, such as for instance strychnine in a small dose, while maximum mydriasis is the consequence of any powerful central excitant, such as strychnine in a large dose.

The degree of spontaneous adrenalinic mydriasis shows the directly proportional intensity of the degree of excitation of the higher nervous centres and, at the same time, on this background, the absence or the great or discreet latency of the photo-motor reflex is to be explained.

## CONCLUSIONS

*Practical therapeutical suggestions for aviation medicine*

In a large dose, strychnine, administered in conditions of high altitude hypobarism, excites the higher nervous centres to the extent that the predominance of central phenomena, which can no longer be compensated by the defence mechanisms of the organism, leads to exhaustion and exitus. In a small dose, strychnine administered in similar conditions of high altitude hypobarism, excites the higher nervous centres to the extent that it stimulates the defence mechanisms of the organism, among which, within the fight of the organism against noxaemia, a paramount role is occupied, particularly by the hyperfunction of the medullo-suprarenal.

These experimental data suggest that the general adaptation capacity of high altitude aviators may be increased during the flight by the administration of small doses of strychnine.

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## LES TROUBLES VISUELS ET LEURS CONSÉQUENCES SUR L'ORGANISME DANS LES CONDITIONS DE PERCEPTION AU DISPOSITIF RADAR

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### METHODE DE RECHERCHE

Toutes les recherches cliniques effectuées sur une échelle internationale ont unanimement démontré que les radiations du radar ne justifient pas les troubles visuels et généraux associés du personnel qui travaille dans ces conditions.

Nos investigations ont tout d'abord précisé les conditions complexes du travail de l'appareil visuel au radar et à ses annexes complémentaires liées à la durée du travail visuel la distance à laquelle s'effectue ce travail visuel et la luminosité des écrans. Après cela nous avons poursuivi avant et comparativement après la fin du travail visuel, les suivants objectifs : l'acuité visuelle la refraction à la skiascopie, la proximométrie avec le proximomètre M. Carapancea

the suprarenal capsule, while the actively liberated adrenaline in a very small quantity and spread throughout the organism by the sanguine way, accompanied by a local ocular factor, with a propensity to glaucoma, determines the *glaucomatous mydriasis*.

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These facts constitute yet another argument in favour of mydriatogenous adrenalinic mechanism, generally a consequence of any central excitant, their different action intensities explain the degree of the mydriatic manifestation, in the sense that the discreet mydriasis is the consequence of any weak central excitant, such as for instance strychnine in a small dose, while maximum mydriasis is the consequence of any powerful central excitant, such as strychnine in a large dose.

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In a large dose, strychnine, administered in conditions of high altitude hypobarism, excites the higher nervous centres to the extent that the predominance of central phenomenon, which can no longer be compensated by the defence mechanisms of the organism, leads to exhaustion and exitus. In a small dose, strychnine, administered in similar conditions of high altitude hypobarism, excites the higher nervous centres to the extent that it stimulates the defence mechanisms of the organism, among which, within the fight of the organism against anoxemia, a paramount role is occupied, particularly, by the hyperfunction of the medullo-suprarenal.

These experimental data suggest that the general adaptation capacity of high altitude aviators may be increased during the flight by the administration of small doses of strychnine.

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générale variant entre 8 et 14 mg et un esthésiogramme de la conjonctive bulbaire à moyenne variant entre 11 et 23 mg c'est à dire — vis à vis de nos recherches antérieures d'esthésiometrie, effectuées au sol de notre pays (1) — avec les seuls supérieurs de ces sensibilités, modérément baissées à la corne et très accentuées à la conjonctive bulbaire, ce qui indique une légère augmentation de la sensibilité cornéenne et une très accentuée augmentation de la sensibilité de la conjonctive bulbaire (Fig 1)

La répartition du pigment retinien maculaire et perimaculaire a rarement présente des déficiences et surtout chez les hypermétropes

Les recherches effectuées ont rendu évidente l'identité des troubles visuels et généraux associés chez tous les hypermétropes des deux premiers groupes à acuité plus accentuée dans le premier groupe comparé au second et l'absence presque complète des mêmes phénomènes au troisième groupe, le marin

Donc également les hypermétropes mis dans l'état de sur sollicitation visuelle manifestent avec le temps — soit dans un bref délai ou bien plus tard après des mois de travail visuel et spécialement en fonction des périodes plus soutenues de travail — toute une série de symptômes subjectifs et objectifs oculaires et généraux associés qui une fois installés se manifestent continuellement au courant de la vie journalière à l'occasion de toute sollicitation de la vue



FIG 1

Esthesiogrammes topographiques moyens de la corne et de la conjonctive bulbaire en mg press on présentés sous forme de résultante générale pour les deux yeux. À gauche chez la normale ( ) À droite chez les hypermétropes qui travaillent soit au radar soit aux planchettes horizontales de près et verticales de distance

(1) Carapancea M Popesco M Ratu E Pintilie I Stoian M Stefan M La sensibilité de la conjonctive bulbaire et de la corne dans des conditions d'hypobarisme chez les pilotes de grande altitude Communication présentée à l'Institut de Physiologie Normale et Pathologique D. Dr. Popescu de l'Académie de la République Populaire Roumaine dans la séance du 15 XII 1960 sous la présidence du Directeur de l'Institut l'Académicien Prof Dr Gr Benetato

( ) Carapancea M Popesco M Ratu E Pintilie I Stoian M Stefan M La sensibilité de la conjonctive bulbaire et de la corne dans des conditions d'hypobarisme chez les pilotes de grande altitude. Communication présentée à l'Institut de Physiologie Normale et Pathologique D. Dr. Popescu de l'Académie de la République Populaire Roumaine dans la séance du 15 XII 1960 sous la présidence du Directeur de l'Institut l'Académicien Prof Dr Gr Benetato

et M. Popesco (1) et l'esthésiometrie cornéenne et conjonctivale bulbaire avec l'esthésiomètre L. Ruiu et A. Ivanovici (2)

Simultanément on a aussi examiné le fond de l'œil pour déterminer la répartition du pigment rétinien maculaire et perimaculaire

Ces recherches ont été effectuées sur 107 travailleurs des stations de radiolocation, âgés de 19 à 33 ans, répartis en trois groupes: le premier groupe forme d'opérateurs de radar, le second groupe d'enregistreurs et lecteurs aux planchettes horizontales, de près et verticales, de distance, et le troisième groupe de radiotelegraphistes et electromecaniciens, et en même temps le groupe témoin vis à vis des deux autres

### RESULTATS DES RECHERCHES

Le premier groupe était constitué de 59 opérateurs de radar, dont 38 hypermétropes, 9 myopes et 12 emmétropes

Le second groupe forme de 22 enregistreurs ou lecteurs aux planchettes horizontales, de près et aux planchettes verticales, de distance, comprenait 12 hypermétropes et 10 emmétropes

Le troisième groupe — témoin vis à vis des deux autres — forme de 26 radiotelegraphistes et electromecaniciens — était constitué de 18 hypermétropes, 2 myopes et 6 emmétropes

Les hypermétropes avaient une acuité visuelle comprise entre 1 et 1,5, la réfraction jusqu'à + 2 d et - 3 d. Les myopes avaient une acuité visuelle comprise entre 1/1,5 et 1/2, la réfraction jusqu'à 1 d et - 2 d.

La proximonétrie, comprise entre 9 et 14 cm, a enregistré, seulement chez les hypermétropes des deux premiers groupes — proportionnellement à l'âge, l'acuité et la réfraction de chaque cas considéré individuellement — un léger rapprochement du punctum proximum

Le mesurage de la sensibilité cornéenne et conjonctivale bulbaire a déterminé aux deux yeux et seulement chez les hypermétropes des deux premiers groupes, un esthésiogramme cornéen à moyenne

(1) Carapancea M. Popesco M. Pintilie I. Stoian M. Teodorescu V. Stefan M.  
Les modifications de l'accommodation visuelle dans des conditions d'hypobarisme chez les pilotes de grande altitude. Communication présentée à l'Institut de Physiologie Normale et Pathologique D. Danielopolu de l'Académie de République Populaire Roumaine dans la séance du 14 V 1960 sous la présidence du Directeur de l'Institut l'Académicien Prof. Dr. Gr. Benetato

(2) Carapancea M. Popesco M. Ruiu E. Pintilie I. Stoian M. Stefan M.  
La sensibilité de la conjonctive bulbaire et de la corne dans des conditions d'hypobarisme chez les pilotes de grande altitude. Communication présentée à l'Institut de Physiologie Normale et Pathologique D. Danielopolu de l'Académie de la République Populaire Roumaine dans la séance du 14 V 1960 sous la présidence du Directeur de l'Institut l'Académicien Prof. Dr. Gr. Benetato

"mal visuel de train" mal visuel d'automobile, mal visuel de fiacre', (c) soit pour suivre le va et vient de la foule dans la rue, avec la sensation de peur des espaces pleins de foule' cirque, etc — sorte d'agoraphobie visuelle — avec la préférence des rues moins peuplées ou même désertes (3)

10 Myodesopsie

11 Photophobie légère au commencement et tenace plus tard

12 Crampes oculaires douloureuses

13 Myalgie légère des droits internes aux mouvements des globes dans l'orbite, à l'occasion de leurs sollicitation l'un après l'autre ou ensemble (3)

14 Douleurs oculaires aux mouvements des globes dans l'orbite (3) (5)

15 Douleurs retro-oculaires (2) (3)

16 Sensation de fatigue palpebrale et oculaire (3) (5)

17 Préférence de garder fréquemment les paupières fermées pour se reposer la vue

18 Nécessité d'appuyer sur les yeux avec les doigts chauffés rapidement à une source proche de chaleur bec, fourneau, calorifère, etc (3)

19 Diplopie passagère sans remission pendant toute la vie, qui apparaît soit au réveil, surtout le matin, comme 'diplopie de bonjour', soit au courant de la journée, en des durées variant de quelques secondes jusqu'à quelques minutes et cessant généralement après un effort de fixation de l'image apparue double (3)

20 Parfois Migraine ophthalmique atypique, fugitive, manifestée par des hémianopsies homonymes partielles des scotomes scintillants atypiques et des céphalées instables en fait de moment d'apparition, durée et siège (3)

21 Parfois Sensation de tension intra orbitaire passagère

22 Parfois Adaptation diurne retardée de 10-15-30 minutes après la sortie de la chambre obscure du radar (3)

23 Parfois Photophobie à la lumière du jour et de la chambre (3)

24 Parfois Adaptation nocturne déficitaire par perception confuse continue à la lumière de nuit (3)

#### GÉNÉRAUX

1 Maux de tête passagers (3)

2 Douleur frontale en barre (1) (2) (3)

3 Douleur aux tempes (3)

4 Céphalée occipitale (3)

5 Céphalée diffuse ténace, d'habitude au courant de la deuxième moitié de la journée ou à la fin de la journée du travail visuel (1) (3) (5)

Ces symptômes au nombre de 59 — dont une part fut décrite aux radaristes par Berest, Gibert, Perdriel (1), Berest, Perdriel, Colin (2), Indekim (4), Visnevski, Petrenko (5), et auxquels j'ajoute les symptômes inédits observés personnellement avec mes collaborateurs Popesco, Stefan, Bengulesco, Musetesco (3) — je les présente dans une systématisation personnelle, selon leur gravité croissante

### Symptomatologie des troubles oculaires et généraux associés

#### Symptômes subjectifs

#### Oculaires

- 1 Sensation de démangeaison conjonctivale passagère (3)
- 2 Sensations de cuisson et de brûlure conjonctivale, passagères (1) (3)
- 3 Larmoiement passager (1) (2) (3) (5)
- 4 Sensation de piqures intra oculaires passagères (1) (2) (3) (5)
- 5 Sensation de tension intra oculaire passagère (1) (2) (3)
- 6 Effacement passager de l'image vue comme à travers un brouillard fugitif (3)
- 7 Aperception visuelle fugitive (3)
- 8 Instabilité de la vision claire de près, passagère au début et accentuée, plus tard, pour lire, dessiner et, en général, suivre tous les détails rapprochés (3)
- 9 Instabilité de la vision claire de loin, passagère, au début et accentuée, plus tard (a) soit pour suivre les images au cinématographe, à la télévision, au théâtre, en amphithéâtre, en classe, etc., avec la préférence de rester au fond de ces différentes pièces, (b) soit pour suivre le défile rapide des maisons, des arbres, des poteaux télégraphiques, etc., vus d'un véhicule en marche, avec les sensations de "mal visuel du passager pendant le décollage et l'atterrissage",

(1) Berest N, Gibert A P Perdriel G. Étude analytique des facteurs d'asthénopie oculaire chez les lecteurs des scopes radar. *La Médecine Aéronautique* 1956 XI, 2 pp 197-214

(2) Berest N Perdriel G Colin J. Étude statistique de la fatigue visuelle des lecteurs du scope radar. *La Médecine Aéronautique* 1958 XIII 2 pp 135-139

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- 18 Lieb W A (1957) Augenhintergrundveränderungen bei Sichelzellanämie. *Ber ophth Ges Heidelberg* 60 308-312
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- 20 Jeandelize P and Drouet, P L. (1936) Troubles endocriniens et plus spécialement hypophysaires dans les hémorragies récidivantes du corps vitré. *Bull Soc ophtal Paris* 260-266
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- 24 Belz and Bouchel (1951) Ultrasonothérapie et hémorragies du vitré. *Arch Ophtal Paris* 11 182
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## GENERAUX

## 1 Vomis ements (3)

2 Parfois Facies de nevrose asthenopique, hypermetropique — instale a la longue et plus evident pendant l'acte de regarder de pres — au suivantes particularites (a) sourcils abaisses à pli vertical du tegument inter sourcilier avec des douleurs consecutives sur sourcilières (b) face legerement contractee ou meme crispee, avec l'aspect concentre du visage (c) myosis avec l'aspect severe du regard

3 Parfois Spasmes faciaux legers, divers, accompagnant les tics blepharo spastiques

4 Parfois Troubles inconstants du rythme cardiaque

5 Parfois — Titubation

N B Si tous les symptomes ci dessus ne se reproduisent pas tous jours on y trouve au moins, toujours 90% de ceux ci

Independamment de l'etat de refraction, nous avons constate parfois et seulement chez les operateurs de radar la diminution de leur capacite sexuelle

## INTERPRETATION DES RECHERCHES

Les troubles polymorphes decrits tant dans la fonction de l'appareil visuel que dans le fonctionnement de tout l'organisme n'apparaissent pas seulement comme des manifestations inexplicables, mais aussi sans liaison aucune entre elles

En realite l'explication de ce polymorphisme symptomatique prend son point de depart dans la continuelle activite de l'appareil visuel hypermetropique qui pour n'importe quelle distance doit toujours former mathematiquement l'image claire sur la rétine

Ce complexe travail, de mise à point continuelle de l'image et qui constitue au fond l'aboutissant visuel de tous les mecanismes oculaires explique la symptomatologie oculaire qui s'y rattache

C'est ainsi que l'on peut expliquer en detail tous les symptomes mentionnes

— La sensation de demangeaison conjonctivale passagere

— Les sensations de cuisson et de brulure conjonctivale, passageres

— L'augmentation esthesometrique legere de la sensibilite corneenne et très accentuee de la sensibilite conjonctivale bulbaire,

Tous ces symptomes sont dus au fait qu'au cours de l'accommodation pour la vision de pres lorsque la frequence du clignement decroit et la circulation palpebro conjonctivale ralentit, il apparait une microstase tant palpebrale à oedème consecutif qu'aussi conjonctivale d'ou la pression exercee par cette microstase sanguine sur les terminaisons nerveuses locales palpebrales et conjonctivales determinent les phenomenes plus haut decrits

— La congestion passagere de la conjonctive palpebrale est un stade plus avance de la microstase sanguine decrite



6 États migraineux non définis (3)

7 État de malaise (3)

8 Vertige d'origine visuelle, passager au commencement et tenace plus tard (1) (3)

9 Hémicranie, du côté de l'œil directeur, soit sur un même fond hypermétrope bilatéral, soit sur un fond anisométrique

10 Inaptitude (3)

11 Nausée discrète au commencement et tenace plus tard (3)

12 Somnolence continuelle et besoin impérieux de dormir après quelques heures de travail visuel (3)

13 Fatigue générale (3) (5)

14 Complexe d'infériorité par incapacité de deviner son interlocuteur, parce que cela provoque "un larmoiement intense" et "une douleur oculaire"

15 États asthénico-dépressifs (3)

16 États d'inquiétude

17 États d'irascibilité (3)

### Symptômes objectifs

#### Oculaires

1 Augmentation esthésiométrique légère de la sensibilité cornéenne et très accentuée de la sensibilité conjonctivale bulbaire (3)

2 Congestion passagère de la conjonctive palpébrale

3 Hyperémie conjonctivale bulbaire, accentuée par le sommeil et améliorée après deux à trois heures de veille (2) (3) (5)

4 Ectasie des vaisseaux de la conjonctive bulbaire (3)

5 Conjonctivite papillaire

6 Conjonctivites frustes guérissant spontanément, au début et à caractère traînant et rebelle, plus tard, aux traitements habituels (3)

7 Congestion légère et fin oedème du bord palpébral (1) (3)

8 Blépharo-conjonctivite à prédisposition aux folliculites ciliaires, orgelets et abcès palpébraux (1) (3) (4) (5)

9 Rapprochement du punctum proximum (2) (3)

10 Parfois Troubles discrets dans la disposition du pigment rétinien des régions maculaire et perimaculaire (3)

11 Parfois Hypertension rétinienne provoquée ou aggravée en cas de préexistence

12 Parfois Tic blépharo-spasmodique

13 Parfois Exophtalmie monolatérale, à peine esquissée et très passagère

La contraction de l'accommodation pour la vision de loin est peu accentuée et se passe lentement en 0 50 jusqu'à 1 16. La contraction de l'accommodation pour la vision de près est maximale et se passe rapidement en 0 39 jusqu'à 0 82 étant en même temps accompagnée encore par deux autres réflexes de l'appareil visuel le réflexe de la convergence et le réflexe du myosis.

Il en résulte que comparée avec la vision de loin la vision de près est plus fatigante puisqu'elle nécessite un mécanisme plus compliqué, basé sur trois réflexes intimement liés entre eux, à savoir le réflexe de l'accommodation pour la vision de près, le réflexe du myosis et le réflexe de la convergence. Cependant le réflexe de l'accommodation pour la vision de près et le réflexe du myosis sont nullement synchrones et le réflexe de l'accommodation pour la vision de près et le réflexe de la convergence gardent chacun sa parfaite individualité puisqu'on peut accommoder pour le regard de près sans converger. Mais le réflexe du myosis s'installe presque synchroniquement avec le réflexe de la convergence puisque le myosis constitue la *synkinésie synergique* trienne liée corticalement ou sous corticalement à la convergence des axes visuelles à partir déjà du quatrième mois.

Le mécanisme de la vue claire, pour la vision de près aussi bien que de loin provoque donc

1 Des efforts accommodatifs continuels qui conduisent à des contractions toniques et très rarement cloniques du muscle ciliaire avec images tantôt confuses tantôt claires, se succédant lentement ou rapidement. Autrement dit il se forme un état d'asthénopie accommodative d'incapacité de perception soutenue par suite de la fatigue du muscle ciliaire continuellement sollicité.

Une très importante mention s'impose à être faite comparative ment entre l'hypermétropie et l'astigmatisme tant hypermétrope simple et composé, que mixte. Celle-ci parce que l'hypercontraction uniforme du muscle ciliaire sur tout le pourtour de sa surface qui se passe dans l'hypermétropie, est bien sûr moins fatigante que l'hypercontraction non uniforme parcellaire seulement d'une seule portion musculaire sur le fond de contraction générale de tout le muscle ciliaire tel que dans l'astigmatisme hypermétrope simple et composé. L'unique hypercontraction segmentaire qui se produit dans l'astigmatisme mixte apparaît donc de ce fait comme moins fatigante que celle des deux variétés d'astigmatisme hypermétrope.

Il résulte donc de ces raisons physiologiques que l'astigmatisme hypermétrope simple ou composé fatigue l'œil de plus que l'hypermétropie simple et que l'astigmatisme mixte fatigue l'œil moins que l'hypermétropie simple.

2 Des contractions triennes un réflexe de myosis pour la vision de près et un réflexe de retour à la normale parfois même une légère mydriase pour la vision de loin.

3 Des contractions de la musculature oculaire extrinsèque réflexe de convergence pour la vision de près réflexe de relâchement

— L'hyperémie conjonctivale bulbaire, accentuée par le sommeil et améliorée après deux à trois heures de veille,

— L'écrysie des vaisseaux de la conjonctive bulbaire,

Ces deux symptômes sont dus au fait que la stase des vaisseaux conjonctivaux est accentuée pendant le sommeil, tant par le ralentissement de la circulation locale que par la chaleur des paupières qui recouvrent l'œil, la stase s'améliore après quelques heures de veille, c'est-à-dire de reprise de la circulation sanguine et de contact avec l'air ambiant plus frais, cependant la stase ne disparaît pas complètement à cause de la reprise de l'acte accommodatif pour la vision de près à fréquence réduite du clignement, d'où cercle fonctionnel vicieux de la circulation locale, qui, avec le temps réalise la microcirculation vasculaire irréversible, donc à conjonctives définitivement congestionnées

— La conjonctivite papillaire,

— Les conjonctivites frustes guérissant spontanément au début et à caractère truant et rebelle plus tard aux traitements habituels,

— La congestion légère et le fin œdème du bord palpébral,

— La blépharo conjonctivite, à prédisposition aux folliculites ciliaires, orgelets et abcès palpébraux,

Ces symptômes sont dus au fait que la stase des vaisseaux conjonctivaux et palpébraux diminue petit à petit la résistance locale envers le microbisme latent — normalement présent — qui de la sorte, en fin de compte, peut exalter sa virulence d'où apparition d'infections de la conjonctive et ensuite du bord palpébral, au début à guérison spontanée et plus tard à caractère définitif et rebelle aux traitements habituels

— Le larmoiement passager est dû au réflexe à point de départ (a) soit de l'irritation cornéco conjonctivale provoquée par leur léger séchage, consécutivement à la fréquence réduite du clignement au cours de l'accommodation soutenue pour la vision de près, (b) soit de l'irritation blépharo conjonctivale inflammatoire, consécutive à la stase des vaisseaux conjonctivaux et palpébraux (c) soit de l'irritation cornéco conjonctivale conjointement à celle blépharo conjonctivale

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Afin de mieux comprendre la physiopathologie des symptômes qui suivent et qui découlent de l'ert fonctionnel du muscle ciliaire, l'élément principal de la vue claire, les suivantes constatations s'imposent dans le cadre de l'accommodation hypermétrope

Chez l'hypermétrope, le muscle ciliaire est sur-sollicité par l'activité accommodative, effort qui lui est imposé sans relâche, tant pour n'importe quelle vision de loin et même pour la vue à l'infini, puisque le punctum remotum est virtuel et situé au delà de l'infini, que surtout pour la vision de près, puisque le punctum proximum est situé derrière la rétine

visuel soutenu de près ainsi qu'en des phénomènes généraux à savoir céphalée vertige somnolence nausée, vomissements, troubles inconstant du rythme cardiaque

À part la conjonctivite aiguë que j'ai guérie en quelques jours je n'ai découvert aucun signe objectif pouvant justifier les troubles généraux dont il se plaignait

Plus tard j'ai eu à ajouter encore à cette observation les trois faits suivants

1 Les troubles généraux s'installaient d'habitude alors qu'il avait rapidement démonté gravis et rassemble les parties de divers autres exercices continuellement répété en vue d'un examen d'armurier militaire

2 Les troubles généraux ont dû paraître pendant quelques jours après les injections intra-orbitaires mais pendant ce temps la vue se voyait toutes les fois qu'il faisait des efforts visuels à l'occasion des exercices pour son futur examen

3 Ce soldat guéri de la conjonctivite avec laquelle il se trouvait présent et chargé de copier des situations sanitaires, se plaignait de nouveau après deux heures de travail des mêmes troubles généraux violents qui étaient mentionnés dans sa fiche médicale

Bien entendu que je n'ai aucunement pensé alors à une relation entre ces phénomènes généraux et son acuité visuelle hypernormale de 125 et son hypermétropie de +2 à 3 ph

Ces trois concours de circonstances qui m'ont paru bizarres, à l'époque deviennent maintenant parfaitement explicables grâce à la connaissance des relations anatomo-physiologiques d'entre l'activité visuelle hypermétrope et l'excitation du ganglion ciliaire à savoir

1 Les troubles généraux c'est à dire les manifestations pathologiques viscérales dépendaient de excitations venant du ganglion ciliaire étant en réalité des réflexes cilio-viscéraux qui apparaissent à la suite d'efforts prolongés de la vision de près

2 L'anesthésie bilatérale des ganglions ciliaires a interrompu les réflexes cilio-viscéraux puisque le ganglion ciliaire était mis en impossibilité de transmettre ces impulsions anormales Pour cette raison et pendant toute la durée de l'anesthésie des ganglions ciliaires, les organes respectifs ont repris leur physiologie normale En même temps la vue se troublait toutes les fois qu'on faisait des efforts visuels de près prolongés le muscle ciliaire se fatiguant invariablement

3 L'effet de l'anesthésie bilatérale des ganglions ciliaires disparaissant et la voie des réflexes cilio-viscéraux se rétablissant l'excitation des ganglions ciliaires pendant l'activité visuelle et spécialement pour le travail de près a provoqué de nouveau les troubles viscéraux liés anatomo-fonctionnellement au ganglion ciliaire

Mais en dehors des réflexes cilio-viscéraux manifestes sous l'aspect des troubles généraux décrits l'excitation du ganglion ciliaire provoque encore d'autres troubles généraux dus cette fois-ci à l'excitation du

de la convergence pour la vision de loin et des alternances de contractions relâchements de la musculature péri oculaire strice a l'occasion des excursions des yeux

Ces trois activités musculaires, exagérées chez l'hypermétrope, déterminent des impulsions nerveuses anormales, qui se transmettent par les filets nerveux respectifs, tant de l'intérieur que de l'extérieur du globe, à la zone réflexogène orbitaire, qui est le ganglion ciliaire (1)

Des recherches expérimentales de l'un d'entre nous ont démontré que les réflexes intéressant divers organes à point de départ oculaire, partent en réalité du ganglion ciliaire, c'est pourquoi on les appelle réflexes cilio viscéraux (1) (2)

La définition de chaque réflexe cilio viscéral (vasculaire, respiratoire, œsophagien, gastrique, intestinal, colique, vésical, glycémique et viscéro moteur en général) comprend l'ensemble des troubles de l'organe respectif consécutifs à l'excitation exercée par le ganglion ciliaire

Ces réflexes, manifestes donc sous l'aspect de troubles généraux à caractère polymorphe, incompréhensible et non liés entre eux, peuvent être expliqués uniquement par l'activité visuelle hypermétropique, qui excitant le ganglion ciliaire engendre les réflexes, plus ou moins forts, des viscères qui en dépendent

À l'appui de ce point de vue, je cite, parmi les observations cliniques personnelles, le résumé de celle qui apparaît la plus impressionnante, vu qu'elle contient aussi les éléments fortuits d'une expérience évidemment démonstrative (3)

Au mois de novembre 1944 — époque où certaines unités militaires venaient de fusionner — il s'est présenté, à l'infirmerie de l'unité où j'étais mobilisé, un soldat, d'une autre unité, auquel — d'après les données notées dans sa fiche médicale — on avait récemment bilatéralement les ganglions ciliaires pour un glaucome aigu bilatéral

Les manifestations du présumé glaucome — diagnostique et traitée par un non spécialiste — consistent en des phénomènes oculaires, à savoir congestion conjonctivale aiguë bilatérale, muqueuse exsudative, avec photophobie et vue trouble intermittente au travail

(1) Carapincea M. Simionescu Carapincea S. Popesco I. Le rôle du système nerveux dans le mécanisme des réflexes à point de départ oculaire. Communication 1<sup>re</sup>. Le point de départ réel des réflexes. Le ganglion ciliaire. Bull. Sc. Méd. de l'Acad. R. P. R., 1954, VI, 4, pp. 769-773

(2) Carapincea M. Simionescu-Carapincea S. Popesco I. Le rôle du système nerveux dans le mécanisme des réflexes à point de départ oculaire. Communication IV e. Les voies des réflexes cilio viscéraux. Bull. Sc. Méd. de l'Acad. R. P. R., 1954, VI, 4, pp. 797-812

(3) M. Carapincea. La névrose hypermétropique. Communication au Congrès National des Sciences Médicales de la République Populaire Roumaine dans le cadre de l'Institut de Physiologie Normale et Pathologique. Daniel Danielopolu de l'Académie de la République Populaire Roumaine dans la séance du 7 mai 1957

visuel soutenu de près ainsi qu'en des phénomènes généraux à savoir céphalée vertige, somnolence nausée vomissements troubles inconstants du rythme cardiaque

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2 Les troubles généraux ont disparu pendant quelques jours après les injections intra orbitaires mais pendant ce temps la vue se voilait toutes les fois qu'il faisait des efforts visuels à l'occasion des exercices pour son futur examen

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Bien entendu que je n'ai aucunement pensé alors à une relation entre ses phénomènes généraux et son acuité visuelle hypernormale de 1/25 et son hypermétropie de + 2 d sph

Ces trois concours de circonstances qui m'ont paru bizarres à l'époque deviennent maintenant parfaitement explicables, grâce à la connaissance des relations anatomo physiologiques d'entre l'activité visuelle hypermétropique et l'excitation du ganglion ciliaire à savoir

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3 L'effet de l'anesthésie bilatérale des ganglions ciliaires disparaissant et la voie des réflexes cilio viscéraux se rétablissant l'excitation des ganglions ciliaires pendant l'activité visuelle et spécialement pour le travail de près a provoqué de nouveau les troubles viscéraux liés anatomo-fonctionnellement au ganglion ciliaire

Mais en dehors des réflexes cilio viscéraux manifestes sous l'aspect des troubles généraux décrits l'excitation du ganglion ciliaire provoque encore d'autres troubles généraux dus cette fois-ci à l'excitation du

cortex cerebral, soit directement par voie cilio corticale, soit indirectement par toutes les voies reliant au cortex les viscères sujets aux troubles cilio viscéraux. Ce genre de troubles généraux ne sont donc autre chose que l'effet des excitations corticales dues aux reflexes cilio corticaux et au reflet cortical de retour des reflexes cilio viscéraux.

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Les considérations ci dessus nous permettent de mieux comprendre la physio pathologie des symptômes qui suivent, et qui découlent de l'état fonctionnel du muscle ciliaire, dans le cadre de l'accommodation hypermetropique

— La sensation de piqures intra oculaires passagères,

— La sensation de tension intra oculaire passagère,

Les deux symptômes sont dus aux contractions fortes et rapides de la musculature intrinsèque oculaire qui provoque de très fines et fugitives hyperophtalmotonies

— Le rapprochement du punctum proximum est dû à l'état de spasme ou crampe accommodative, c'est à dire à l'état de contracture soutenue du muscle ciliaire, qui manifeste de la sorte un spasme myopigène

— L'effacement passager de l'image vue comme à travers un brouillard fugitif,

— L'aperception visuelle fugitive,

— L'instabilité de la vision claire de pres, passagère, au début et accentuée, plus tard, pour lire, dessiner et, en général, suivre tous les détails rapprochés,

— L'instabilité de la vision claire de loin, passagère, au début et accentuée, plus tard (a) soit pour suivre les images au cinématographe, à la télévision, au théâtre, en amphithéâtre, en classe, etc, avec la préférence de rester au fond de ces différentes pièces, (b) soit pour suivre le défile rapide des maisons, des arbres des poteaux télégraphiques, etc, vus d'un véhicule en marche, avec les sensations de mal visuel du passager pendant le décollage et l'atterrissage, mal visuel de train, mal visuel d'automobile mal visuel de fiacre, (c) soit pour suivre le va et vient de la foule dans la rue, avec la sensation de peur des espaces pleins de foule (cirque, etc) — sorte d'agoraphobie visuelle — avec la préférence des rues moins peuplées ou même désertes

— Le vertige d'origine visuelle passager au commencement et tenace plus tard,

— Parfois La titubation,

Tous ces symptômes sont dus à l'alternance de contraction et de relâchement du muscle ciliaire et en général à l'état d'asthénopie — état dans lequel la vue est incapable d'une application soutenue — et

en special a l'etat d'asthenopie accommodative c'est a dire a l'asthenopie qui survient dans l'hypermetropie a la suite de la fatigue causée par l'accommodation autrement dit l'asthenopie accommodative c'est l'etat d'incapacite de contraction du muscle ciliaire dans les intensites correspondentes à la mise a point de l'image

— La myodesopsie ou les mouches volantes representent l'apparition dans le champ visuel des micro scotomes positifs mobiles, comme des points noirs isoles ou agglomérés en chaine ou en amas, il s'agit des elements figures du sang qui — passant à travers les stomates des vaisseaux des proces ciliaires au cours de leurs variables tensions determinees par les mouvements accommodatifs du muscle ciliaire — sont arrives dans le corps vitre, ou, bien qu'invisibles a l'ophthalmoscope par leurs mouvements selon les lois combinees de l'inertie et de la gravitation des corps legers dans les liquides, ils provoquent par leurs ombre projetee sur la retine la sensation visuelle decrite

Ce phenomene apparait donc facilement explicable dans l'hypertension retinienne provoquee ou aggravee en cas de preexistence

— La photophobie legere au commencement et tenace plus tard, est due en partie a la contraction penible et meme douloureuse des muscles irien et ciliaire fatigues deja par l'accommodation

— Les crampes oculaires douloureuses

— La myalgie legere des droits internes aux mouvements des globes dans l'orbite, a l'occasion de leurs sollicitations l'un apres l'autre ou ensemble

— Les douleurs oculaires aux mouvements des globes dans l'orbite

— Les douleurs retro oculaires

— La diplopie passagere sans remission pendant toute la vie, qui apparait soit au reveil surtout le matin comme diplopie de bonjour soit au courant de la journee en des durees variant de quelques secondes jusqu'a quelques minutes et cessant generalement apres un effort de fixation de l'image apparue double

Tous ces symptomes sont dus a la sur sollicitation synchrone a l'acte accommodatif de la musculature peri oculaire strice C'est ainsi que la diplopie passagere et sans remission pendant toute la vie doit etre consideree specialement comme une manifestation typique de la fatigue extreme des muscles convergents sur sollicites en opposition a la diplopie temporaire par deplacement du globe du à la paralysie oculo-motrice ou a une bride cicatricielle dont la fausse image est atténuee ou disparait par accoutumance neutralisation ou guerison La myalgie accentuee des droits internes se manifeste surtout comme suite des efforts energetiques et repetes de convergence qui tendent a situer en strabisme convergent consecutif les yeux hypermetropiques Si a l'etat de contracture de la musculature peri-oculaire s'ajoute aussi une



tenonite rhumatismale ou même une cellulite orbitaire, les deux discrètes, alors on s'explique pourquoi les douleurs oculaires et retro oculaires deviennent extrêmement violentes au cours des mouvements des globes oculaires.

— Il y a nécessité d'appuyer sur les yeux avec les doigts chauffés rapidement à une source proche de chaleur : bec, fourneau, calorifère, etc., est due au fait que la pression sur un muscle spasme le décontracte et en même temps la chaleur aide au rétablissement de la circulation locale.

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— Parfois l'ectopie blépharo spastique,

— Parfois l'ectopie de neurose asthénopique, hypermétropique— installe à la longue et plus évident pendant l'acte de regarder de près — aux suivantes particularités (a) sourcils abrutis à pli vertical du tégument inter sourcilier avec des douleurs, consécutives sur sourcillères, (b) fice légèrement contractée, ou même crispée, avec l'aspect concentré du visage, (c) myosis avec l'aspect sévère du regard.

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Tous ces symptômes sont le résultat du processus physiologique normal de baisse temporaire de la capacité de travail de la musculature intra et extra oculaire ainsi que de leurs innervations, conjointement avec celle de la fice consécutivement aux activités conjuguées, particulières, précitées par celles-ci. La fatigue de la musculature extra oculaire prend son origine dans les mouvements du globe oculaire poursuivant l'image. Ainsi des enregistrements cinématographiques ont démontré qu'au cours de l'observation au radar, l'œil ne suit pas continuellement le spot lumineux en mouvement sur l'écran, mais se déplace d'une manière désordonnée effectuant un nombre considérable de mouvements alternatifs dans toutes les directions (circulaire linéaire ou combinée), en secousses plus ou moins rapides, d'amplitude et fréquences variables. L'attention soutenue que demande le rythme toujours rapide, dans lequel se succèdent, en un très bref laps de temps, ces stimulus répétés, provoque une instabilité progressive de fixation qui mène à l'épuisement de la fonction visuelle <sup>(1)</sup> <sup>(2)</sup>

— Les maux de tête passagers,

— La douleur frontale en barre,

— La douleur aux tempes,

(1) Berest N. Gilbert A. P. Perdnel C. Étude analytique des facteurs d'asthénopie oculaire chez les lecteurs de scopes radar. La Médecine Aéronautique 1956 N° 2 pp 157-211.

(2) Berest N. Gilbert A. P. Perdnel G. Prévention de la fatigue visuelle chez les lecteurs de scope radar. La Médecine Aéronautique 1956 N° 4 pp 403-412.

# PATHOGENESIS AND AETIOLOGY OF EALES'S DISEASE

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The pathogenesis and aetiology of Eales's disease have been well summarised in several recent papers, such as those of Jefferson and Cloake, 1952, Elliot, 1954, Kimura, Carricker and Hogan, 1956, White, 1961, and especially those of Donders, 1958 and Godde Jolly, 1961, and they have much simplified the task of preparing my own account and interpretation of these complex problems

Eales's disease is originally described in 1880-2 — recurrent peripheral retinal haemorrhages in young males — cannot now be regarded as an entirely separate entity, for many cases have since been described in which the central vessels of the fundus were primarily involved (Gilbert, 1913 a,b, Siegrist, 1913, Davis, 1920, Bullntyne and Michaelson, 1937) In a particularly instructive case—a boy of 14 years old — reported by Lyle and Wybar (1961) the disease was peripheral in one eye and central in the other, which would seem to identify both types as manifestations of the same underlying condition. Nor can it be said that the disease is confined to young males for numerous cases of older ages and both sexes have been described. Nevertheless it remains true that the disease occurs typically in the peripheral retina and that young males are predominantly affected, and I feel it would be wiser to retain the eponymous and noncommittal name of Eales's disease, rather than adopt the later term of "retinal vasculitis". First, because retinal vasculitis is a histopathological finding which is not necessarily synonymous with the ophthalmoscopic observation of retinal sheathing, secondly, because histopathological examination of cases of Eales's disease have not always shown a vasculitis, and, thirdly, because retinal vasculitis is common in ocular pathology quite apart from Eales's disease.

Retinal vasculitis, for instance, may frequently be demonstrated histologically in endophthalmitis from any cause, or in association with uveitis of such widely differing aetiology as sarcoidosis, syphilis, sympathetic ophthalmitis (Eccheverria, 1922) or phacoanaphylactic reactions. An attempt has been made to segregate this group as "secondary vasculitis" to differentiate it from "primary vasculitis" or Eales's disease, but we cannot yet rule out the possibility that Eales's disease may itself be secondary to uveitis, especially anterior uveitis. This association has frequently been noted in the past, and

- La cephalée occipitale
- La cephalée diffuse tenace, d'habitude au courant de la deuxième moitié de la journée ou à la fin de la journée du travail visuel,
- Les états migraineux non définis
- L'état de malaise,
- L'hémicrame du côté de l'ocul directeur soit sur un même fond hypermétrope bilatéral soit sur un fond anisométrique,
- Parfois La migraine ophtalmique atypique fugitive manifestée par des hémianopsies homonymes partielles des scotomes scintillants atypiques et des cephalées instables en fait de moment d'apparition duree et siege
- La somnolence continuelle et le besoin impérieux de dormir après quelques heures de travail visuel
- La fatigue générale
- Le complexe d'infériorité par incapacité de devisager son interlocuteur parce que cela provoque un larmoiement intense et une douleur oculaire
- Les états asthénico dépressifs
- Les états d'inquiétude
- Les états d'irascibilité

Tous ces symptômes sont dus à l'excitation centrale réalisée à son tour par les incitations du ganglion ciliaire transmises au cortex, soit par voie directe cilio corticale soit par voies indirectes reliant au cortex les viscères sujettes aux troubles réflexes cilio viscéraux ces troubles réflexes expliquent et justifient en fin de compte les quatre derniers complexes psychiques

- L'inappétence
- La nausée discrète au commencement et tenace plus tard
- Les vomissements

Tous ces symptômes sont dus aux réflexes cilio digestifs

— Parfois L'hypertension rétinienne provoquée ou aggravée en cas de préexistence

- Parfois Les troubles inconstants du rythme cardiaque

Ces deux symptômes sont dus aux réflexes cilio-vasculaires

En ce qui concerne spécialement l'hypertension rétinienne il faut retenir que la névrose du travail visuel intense et minutieux de l'hypermétropie non corrigée

1 Peut devenir la cause d'une hypertension artérielle générale, qui se manifeste au fond de l'œil comme toute angiopathie rétinienne hypertensive réversible

2 Aggrave l'hypertension artérielle générale en évolution et se manifeste au fond de l'œil sous une forme beaucoup plus marquée qu'elle ne le serait si la même hypertension n'était pas aggravée par la névrose hypermétrope

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— Les maux de tête passagers,

— Il y a douleur frontale en barre

— La douleur aux tempes,

(1) Berest N. Gibert A. P. Peidriel C. Étude analytique des facteurs d'asthénopie oculaire chez les lecteurs de scopes radar. La Médecine Aéronautique 1956 N° 2 pp 197-214

(2) Berest N. Gibert A. P. Peidriel G. Prévention de la fatigue visuelle chez les lecteurs de scope radar. La Médecine Aéronautique 1956 N° 4 pp 403-412

attirent en même temps l'attention que la durée d'adaptation visuelle est de beaucoup supérieure à celle de l'adaptation auditive. Ils démontrent que le bruit des moteurs doit toujours être compris entre 85 et 95 db globaux c'est à dire au dessous des valeurs qui provoquent l'inadaptation de la vue. Mais Svetlakov et Bolsakov (1) dans leur étude de 1957, démontrent que la diminution de l'ouïe aux travailleurs des stations de radiolocation est le résultat de la fatigue de l'analyste auditive à cause de l'action du bruit monotone non interrompu, qui dépasse la valeur du seuil moyen de l'action préjudiciable du bruit qui est de 75 db de sorte que après une journée de travail la majorité présentaient l'acuité auditive diminuée chez toutes les fréquences de 5 à 25 db.

Toujours dans le cadre de la vue hypermétrope c'est aussi intéressant de connaître l'état fonctionnel de la rétine vis à vis du régime de la lumière de la chambre obscure du radar. Zubov (2) en 1958 est arrivé à la conclusion que sous l'influence de la fatigue visuelle les seuils de la sensibilité de contraste augmentent d'habitude.

Mais d'autre part il ne faut pas oublier que dans la chambre obscure du radar il existe une très petite différence d'illumination entre le radar (1-2 lux) l'appareil azimutal (3 lux) et le goniomètre (6 lux) donc de l'ordre de quelques lux.

Les conditions visuelles de travail au radar sont donc tout à fait spéciales. On pense que pour le travail de finesse visuelle qu'il convient en typographie horlogerie gravure couture au fil blanc sur le blanc etc. il s'impose 100 à 250 lux.

On sait que l'accommodation à une faible lumière est normale, mais la désaccommodation est difficile.

Cette situation doit être liée à la constatation qu'au début du crépuscule—lorsque diminue la capacité du sens lumineux—l'accommodation manifeste la tendance vers la refraction de type myopique nocturne.

Donc le régime de lumière identique de la chambre obscure du radar maintient constante l'adaptation de l'œil pendant le travail et lui évite en quelque sorte de ce point de vue la fatigue.

\* \* \*

Afin de mieux comprendre en détail le symptôme suivant qui indique une très étroite liaison entre l'excitation lumineuse et les gonades les suivantes constatations s'imposent dans le cadre de l'observation sur les écrans radar.

(1) Svetlakov M. I. Bolsakov A. M. Sur la sensibilité auditive aux travailleurs des stations de radio-location. *Voенно Meditsinski Journal* 1957 9 pp 31-34.

(2) Zubov V. F. Évaluation de la fatigue visuelle. *Voенно Meditsinski Journal* 1958 10 pp 53-55.

— Parfois l'exophtalmie mono latérale a peine esquissée et très passagère, est due aux reflexes cilio corticaux a effet hypertonique sur la musculature oculaire extrinseque strice, hypertonic qui persiste seulement tant que des impulsions excitatrices agissent sur la region cortico oculomotrice du cote de l'exophtalmie. L'hypertonie passagere de la musculature oculaire extrinseque strice explique d'ailleurs — même en l'absence de l'exophtalmie — la sensation de tension intra orbitaire passagère

— L'adaptation diurne retardée de 10-15-30 minutes, apres la sortie de la chambre obscure du radar,

— La photophobie a la lumiere du jour et de la chambre,

— L'adaptation nocturne deficitaire, par perception confuse continuelle a la lumiere de nuit,

Tous ces symptomes sont dus a l'insuffisance gradée de regeneration de l'erythroptine, au cours de l'acte visuel hypermetropique. Ainsi l'hesperanopie ou la cecite crepusculaire ou l'amblyopie crepusculaire ou l'hypoadaptation retinienne ou l'hemeralopie ou la nyctalopie ou la cecite nocturne est la diminution considerable de la vue installee en même temps que la diminution de la lumiere (crepuscule), consecutivement aux troubles fonctionnels invisibles a l'ophthalmoscope

— Les troubles discrets dans la disposition du pigment retinien des regions maculaire et peri maculaire, sont dus aux troubles anatomiques, visibles a l'ophthalmoscope, dans le cadre de l'hesperanopie

Il faut souligner le fait que les facteurs generaux admis pour l'hesperanopie majeure sont la chorio retinite, la retinite, l'hypovitaminose A, et pour l'hesperanopie mineure ce sont les ametropies et le traumatisme lumineux repeté

Mais nous attirons l'attention, que l'adaptation a l'obscurité peut encore étre empêché aussi par l'inhibition que provoque l'excitant acoustique sur l'humaine

Dans ce sens Visnevski en 1936, Bogoslavski en 1936 et 1939 Kravkov en 1945 et Semenovskii en 1946 [cités par Sneakin et Anisimova (2)] ont constaté que les excitations acoustiques diminuent la sensibilite a la lumiere. A leur tour, Grognot et Perdriel (1) ont constaté en 1959, que le bruit experimental, choisi de la gamme sonore de l'ambiance d'atelier, diminue fortement la capacite visuelle nocturne, ce fut influence en general les travailleurs de nuit, qui doivent conduire des voitures bruyantes et qui risquent de provoquer des accidents de transport et de circulation et influence spécialement les travailleurs des équipes de nuit qui travaillent dans les zones d'ombre dans lesquelles la discrimination de formes est très difficile. Les auteurs

(1) Grognot P Perdriel G Influence du bruit sur certaines fonctions visuelles La Méd Aéron 1959 14 1 pp 25-30

(2) Sneakin P G Anisimova A P Action des excitations inducées (secondaires) sur la sensibilite a la lumiere Fiziologicheskii Journal URSS 19 4, 41 5, p 625

faible et moyenne hypermetropie du radariste, prend souventes fois un aspect dramatique

En general tous les radaristes sujets aux troubles de l'asthenopie accommodative et parmi ceux-ci specialement les hypermetropes exasperes par l'impossibilite de clairement voir les images au cours de leur vie journaliere accusent la lumiere en general et surtout la lumiere artificielle comme cause de leurs troubles visuels

Les brefs et frequents repos accommodatifs que ces ametropes asthenopiques s'imposent suppriment rapidement les troubles de la vue qui cependant reapparaissent aussitot que le travail visuel journalier est repris

Mais pas seulement la non correction de ces vices de refraction engendre la nevrose asthenopique

Aussi l'hypocorrection hypermetropique peut amener de graves desordres de nevrose asthenopique

À son tour l'hypercorrection hypermetropique l'hypercorrection miopique qui transforme l'oeil en hypermetrope, ou l'inexacte correction de l'astigmatisme peuvent provoquer ou — en cas de preexistence — aggraver la nevrose asthenopique

Connaissant le polymorphisme symptomatique de l'asthenopie accommodative en general et specialement provoque par l'hypermetropie on a la possibilite d'insinuer de nombreux faux diagnostics — tels que glaucome tumeur cerebrale, meningite sinusite crises d'hyperthyroidisme diverses psychopaties — ainsi qu'en meme temps de decouvrir le substratum materiel et de la paresse visuelle et des troubles generaux qui s'y rattachent

Ainsi par exemple l'hémicranie du cote de l'oeil directeur soit sur un meme fond hypermetropique bilatéral soit sur un fond anisometropique doit toujours être suspectée comme d'origine asthenopique avant meme de penser à un glaucome

Mais il faut aussi tenir compte du fait que la nevrose asthenopique peut soit aggraver des maladies preexistantes oculaires ou generales dont l'acutisation des symptomes n'a pu être rapportee jusqu'à present à leur vraie cause soit favoriser l'apparition de ces maladies ou justifier le mecanisme inconnu de certaines autres maladies

Pour ce qui est de l'aggravation des maladies oculaires ou de leur favorisation toute infection conjonctivale et palpebrale — pour prendre le plus simple exemple — rebelle à la therapeutique habituelle ou apparue intempestivement doit nous suggerer un fond biologique oculaire au dessous de la normale qui permet aux microbes habituels de s'exacerber la virulence ce qui est evidemment du d'abord à la fatigue de l'appareil visuel en entier qui engendre l'asthenopie accommodative et ensuite à la fatigue generale qui decoule des troubles à point de depart du ganglion ciliaire

Pour ce qui est de certaines maladies digestives à savoir colites gastrites ulceres gastriques et duodenaux celles-ci ont beneficie de la correction dioptrique respective qui a pu soit ameliorer soit même reduire

Le fait que la lumière influence la fonction gonadotrope de l'hypophyse a été démontré en 1937 par J. Benoit et l'influence de la lumière et de la température, dans le déterminisme des modifications saisonnières de la sécrétion d'hormone gonadotrope hypophysaire a été mise en évidence en 1939 par Kabak et Tereza (1)

D'autres recherches, étudiant les suites de l'excitation du nerf optique sur l'hormonogénèse adeno hypophysaire, ont démontré que l'excitation du nerf optique, avec un courant d'induction, ou l'illumination de l'œil avec une lumière monochromatique, modifie d'une manière réflexe la fonction mélanophore et gonadotrope de l'hypophyse (2), tandis que l'hypophysectomie pratiquée à la *Rana temporaria* adulte provoque l'inhibition du cycle sexuel, l'involution des glandes génitales et la régression totale des caractères sexuels secondaires [Gallien cite par Vivien et Schott (3)]

L'application pratique des actions stimulatrices de la lumière est actuellement largement utilisée en zootechnie pour l'augmentation de la production des œufs aux volailles (4) (5), pour l'augmentation de la fécondité et de la production de lait aux vaches (6), dans le même ordre d'idées, il apparaît comme très intéressante l'observation que de tous les cochonnets mis dans de différentes conditions de lumière, le groupe de ceux maintenus dans des boîtes lumineuses manifeste une importante augmentation de leur poids hypophysaire et testiculaire (5)

Les faits ci-dessus exposés nous montrent l'influence que peut avoir la présence de l'excitation lumineuse sur les gonades par l'intermédiaire de l'hypophyse

C'est ainsi que nous pouvons nous expliquer le symptôme rencontré chez quelques-uns des opérateurs de radar à savoir la diminution de la capacité sexuelle

En vérité, celle-ci paraît justifiée par l'absence de l'excitation lumineuse normale sur la fonction gonadotrope de l'hypophyse, au cours du séjour prolongé et pendant longtemps, dans la chambre obscure du radar

#### *Diversité clinique de la névrose asthénopique*

L'asthénopie accommodative de tout astigmatisme mixte, de tout astigmatisme hypermétrope simple et composé, ainsi que surtout de la

(1) Kabak I. M. Tereza S. I. Travaux sur la dynamique du développement Medghiz 1939 II

(2) Sudakov A. D. Les thèses du rapport de la session scientifique L'hypophyse (Physiologie pathologie clinique) 18-21 XII 1957 Medghiz

(3) Vivien J. H. Schott J. Contribution à l'étude des corrélations hypothalamo-pituitaires chez les batraciens. Le contrôle de l'activité gonadotrope Journ. de Physiologie 1958 L 2 pp 561-563

(4) Borison V. A. Izotnovodstvo 1958 4 p 80

(5) Karapetian S. K. DAN URSS 1954 3 p 585

(6) Svecin K. B. Refer. J. Biol. 1957 III p 435



2 Admission des hypermetropes corrigés jusqu'à + 1.5 d sph, dans les suivantes conditions

(a) La distance d'entre l'œil et l'écran radar doit être de 30 jusqu'à 40 cm et pour empêcher une plus grande proximité de l'écran (2) donc pour éviter la sur accommodation inutile, il s'impose un limiteur de tête (4)

(b) Les punctums proximus (1) de l'accommodation ne doivent pas dépasser 13 cm à 20 ans, 16 cm à 30 ans et 24 cm à 40 ans et de la convergence ne doit pas dépasser 11 cm

(c) La durée du travail accommodatif sera de 1 1/2 jusqu'à 2 heures

(d) L'amélioration des déficiences conjonctivales et cornéennes par alimentation abondante en vitamine B<sub>2</sub> qui entretient la vitalité de la conjonctive et de la cornée la carence de cette vitamine aggravant les troubles conjonctivaux décrits consécutivement à la stase des vaisseaux locaux et réalisant ici un punctus minoris resistentiae favorable aux dégénérescences combinées aux infections (2)

(e) L'amélioration de la fatigue accommodative par alimentation riche en vitamines B<sub>2</sub> et C la vitamine B<sub>2</sub> — selon Sisy (3) augmente rapidement l'amplitude de l'accommodation après 30 minutes depuis l'injection et dure jusqu'à 4-5 jours la dose journalière normale nécessaire pour l'homme actif étant de 2 mg la vitamine C possède l'action de maintenir augmentée l'amplitude de l'accommodation, la dose journalière normale nécessaire pour l'adulte étant de 30 à 75 mg

A B Les affections qui impliquent l'élimination ou la non résorption de ces vitamines sont contre indiquées dans la sélection des radaristes (2)

(f) Le repos accommodatif pour le reste de la journée par le port obligatoire permanent des lunettes respectives de correction pour le près par le regard à grande distance — qui relâche le muscle ciliaire — des paysages lointains et par le sommeil (2)

II Dans le cadre thérapeutique général de la névrose asthénopique, les mesures à prendre sont les suivantes

#### A MESURES A APPLICATION STRICTEMENT OCULAIRE

1 Lentilles correctes Au commencement il se peut que la correction optique aggrave même un peu les réflexes cilio viscéraux parce que le muscle ciliaire se contracte à peu près toujours avec la même intensité qu'avant et les verres augmentent donc passagèrement l'amétropie, d'où exagération de ces réflexes

Une à deux semaines constituent en général la période nécessaire pour s'habituer aux lunettes après quoi les malades bien portants prennent parfois même du poids

D'autre part il faut savoir que les lunettes prescrites pendant toute maladie en général et asthénisante spécialement — lorsque le tonus du muscle ciliaire était diminué — sont plus fortes que celles

*le temps de la guérison de ces maladies, ou les deux ensemble, ce qui démontre que la présence des réflexes cilio digestifs empire ces maladies, soit en les aggravant, soit en leur prolongeant le temps de la guérison, ou les deux ensemble*

Il reste à étudier si, en fin de compte, ces réflexes cilio digestifs ne servent pas capables de provoquer même *per primam* la lésion organique des maladies digestives ci dessus citées<sup>1</sup>

Les réflexes cilio corticaux, qui naissent en même temps, aggravent ces symptômes et compliquent parfois ces maladies par des phénomènes de neurose asthénique sans ou avec manifestations psychopathiques

Mais jusqu'ici on a seulement tenu compte de ce que peut provoquer la neurose asthénique

Il devient donc nécessaire de signaler aussi l'apparition de cette neurose sous l'influence des affections asthénisantes, à savoir l'hépatite épidémique, la grippe, les maladies infectieuses chroniques, l'avitaminose, les opérations, la convalescence terminée après infections graves et tout autre motif qui détermine la baisse de l'état général

### *Thérapeutique des troubles visuels et généraux associés engendrés par le radar*

1 La correction dioptrique, qui s'impose en premier lieu, donne des résultats impressionnants de récupération de la santé générale et de la capacité de travail visuel en particulier

En adoptant les idées de Berest, Curveille, Perdriel (1), Visnevski, Petrenko (4), Siva (cité par 3), et ajoutant d'autres, avec mes collaborateurs Popesco, Stefan, Bengulesco, Muscatesco, nous avons établi les suivantes mesures thérapeutiques (2)

1 Vérification minutieuse de l'acuité visuelle, après quoi on décide a L'élimination (1) des hypermétropes au dessus de + 1,5 d sph, des astigmatismes hypermétropiques simples et composés, des astigmatismes myopiques simples au dessus de - 1 d sph et composés, des astigmatismes mixtes, b L'admission (1) des emmétropes, des hypermétropes jusqu'à + 1,5 d sph, mais toujours corrigés, des astigmatismes myopiques simples conformes à la règle et inférieurs à - 1 d, des myopes de - 1 d sph - 2 d sph, - 3 d sph sans choroidose, qui sont les plus indiqués de ceux à l'acuité visuelle pour chaque œil de 1/2 sans correction jusqu'à 9/10 avec correction

(1) Berest N Curveille J Perdriel G Les normes d'aptitude visuelle des lecteurs de scope radar La Médecine Aéronautique 1958 VIII 3 pp 26-27

(2) Caripancea M Popesco M Stefan M Bengulesco D Muscatesco St Les troubles visuels et leurs conséquences sur l'organisme dans les conditions de perception au dispositif radar Communication présentée à l'Institut de Physiologie Normale et Pathologique D Danielopolu de l'Académie de la République Populaire Roumaine, dans la séance du 1 VI 1961 sous la présidence du Directeur de l'Institut l'Académicien Prof Dr Gr Benetato

(3) Mutze K Die Akkommodation des menschlichen Auges Berlin Akademie-Verlag 1956 pp 137

(4) Visnevski N A Petrenko G S Observations ophtalmologiques sur les travailleurs des stations de radiolocalisation Voenno Meditsinski Journal 1958 10 pp 53-55

2 Admission des hypermetropes corrigés jusqu'à + 1.5 d sph dans les suivantes conditions

(a) La distance d'entre l'œil et l'écran radar doit être de 30 jusqu'à 40 cm et pour empêcher une plus grande proximité de l'écran (2) donc pour éviter la suraccommodation inutile il s'impose un limiteur de tête (4)

(b) Les punctus proximus (1) de l'accommodation ne doivent pas dépasser 13 cm à 20 ans 16 cm à 30 ans et 24 cm à 40 ans et de la convergence ne doit pas dépasser 11 cm

(c) La durée du travail accommodatif sera de 1 1/2 jusqu'à 2 heures

(d) L'amélioration des déficiences conjonctivales et cornéennes par alimentation abondante en vitamine B<sub>2</sub> qui entretient la vitalité de la conjonctive et de la cornée la carence de cette vitamine aggravant les troubles conjonctivaux décrits consécutivement à la stase des vaisseaux locaux et real'ant un punctus minoris resistentiae favorable aux dégénérescences combinées aux infections (2)

(e) L'amélioration de la fatigue accommodative par alimentation riche en vitamines B<sub>1</sub> et C la vitamine B<sub>1</sub> — selon Sysy (3) augmente rapidement l'amplitude de l'accommodation après 30 minutes depuis l'injection et dure jusqu'à 4-5 jours la dose journalière normale nécessaire pour l'homme adulte est de 2 mg, la vitamine C possède l'action de maintenir augmentée l'amplitude de l'accommodation, la dose journalière normale nécessaire pour l'adulte étant de 30 à 75 mg

A B Les affections qui impliquent l'élimination ou la non résorption de ces vitamines sont contre indiquées dans la sélection des radaristes (2)

(f) Le repos accommodatif pour le reste de la journée par le port obligatoire permanent des lunettes respectives de correction pour le pres par le regard à grande distance — qui relâche le muscle ciliaire — des paysages lointains et par le sommeil (2)

II Dans le cadre thérapeutique général de la névrose asthénopique, les mesures à prendre sont les suivantes

#### A MESURES A APPLICATION STRICTEMENT OCULAIRE

1 *Lentilles correctes* Au commencement il se peut que la correction optique aggrave même un peu les réflexes cilio viscéraux, parce que le muscle ciliaire se contracte à peu près toujours avec la même intensité qu'avant et les verres augmentent donc passagèrement l'amétropie d ou exagération de ces réflexes

Une à deux semaines constituent en général la période nécessaire pour s'habituer aux lunettes après quoi les malades bien portants prennent parfois même du poids

D'autre part il faut savoir que les lunettes prescrites pendant toute maladie en général et asthénisante spécialement — lorsque le tonus du muscle ciliaire était diminué — sont plus fortes que celles

le temps de la guérison de ces maladies, ou les deux ensemble, ce qui démontre que la présence des réflexes cilio digestifs empire ces maladies, soit en les aggravant, soit en leur prolongeant le temps de la guérison, ou les deux ensemble.

Il reste à étudier si, en fin de compte, ces réflexes cilio digestifs ne seraient pas capables de provoquer même *per primum* la lésion organique des maladies digestives ci dessus citées!

Les réflexes cilio corticaux, qui naissent en même temps, aggravent ces symptômes et compliquent parfois ces maladies par des phénomènes de névrose isthénique sans ou avec manifestations psychopathiques.

Mais jusqu'ici on a seulement tenu compte de ce que peut provoquer la névrose isthénopique.

Il devient donc nécessaire de signaler aussi l'apparition de cette névrose sous l'influence des affections asthénisantes, à savoir l'hépatite épidémique, la grippe, les maladies infectieuses chroniques, la tuberculose, les opérations, la convalescence trépidante après infections graves et tout autre motif qui détermine la baisse de l'état général.

#### *Thérapeutique des troubles visuels et généraux associés engendrés par le radar*

1. La correction dioptrique, qui s'impose en premier lieu, donne des résultats impressionnants de récupération de la santé générale et de la capacité de travail visuel en particulier.

En adoptant les idées de Berest, Curveille, Perdril (1), Visnevski, Petrenko (4), Sisi (cité par 3), et ajoutant d'autres, avec mes collaborateurs Popesco Stefan, Bengulesco, Musetesco, nous avons établi les suivantes mesures thérapeutiques (2).

a. Vérification minutieuse de l'acuité visuelle, après quoi on décide : a. L'élimination (1) des hypermétropes au dessus de + 1,5 d sph, des astigmatés hypermétropiques simples et composés, des astigmatés myopiques simples au dessus de - 1 d sph et composés, des astigmatés mixtes, b. L'admission (1) des emmétropes, des hypermétropes jusqu'à + 1,5 d sph, mais toujours corrigés, des astigmatés myopiques simples, conformes à la règle et inférieurs à - 1 d, des myopes de - 1 d sph - 2 d sph, - 3 d sph, sans choroidose, qui sont les plus indiqués, de ceux à l'acuité visuelle pour chaque oeil de 1/2 sans correction jusqu'à 9/10 avec correction.

(1) Berest N. Curveille J. Perdril G. Les normes d'aptitude visuelle des lecteurs de scope radar. La Médecine Aéronautique 1958 XIII 3 pp 265-270.

(2) Carapanca M. Popesco M. Stefan M. Bengulesco D. Musetesco St. Les troubles visuels et leurs conséquences sur l'organisme dans les conditions de perception au dispositif radar. Communication présentée à l'Institut de Physiologie Normale et Pathologique D. Danielopolu de l'Académie de la République Populaire Roumaine dans la séance du 1 VI 1961 sous la présidence du Directeur de l'Institut l'Académicien Prof. Dr. Gr. Benetato.

(3) Mutze K. Die Akkommodation des menschlichen Auges. Berlin Akademie-Verlag 1956, pp 137.

(4) Visnevski N. A. Petrenko G. S. Observations ophtalmologiques sur les travailleurs des stations de radiolocation. Voenno Meditsinski Journal 1958 10 pp 33-35.

strengthened again recently by Davenport (1954) who pointed out that both retina and uvea may be inflamed together or alternately, and by Godde Jolly (1961) who observed uveitis in 30 per cent of his cases. In fact the significance of this relationship may be missed since long intervals may separate the two inflammations. A further difficulty is that retinal vasculitis of the kind seen in multiple sclerosis which is not secondary to uveitis, and would therefore have to be classified as 'primary', is certainly not in the same clinical category as Eales's disease.

# **PATHOLOGY**

In considering the pathogenesis of Eales's disease we are much handicapped by the difficulty in obtaining pathological material at a sufficiently early stage to determine the natural history of the disease or even to decide with certainty whether it may have a single cause or multiple causes. Most of the globes which have been examined histologically had been removed in the final stages of retinal detachment or of glaucoma when the usual process may well have long subsided. Donders (1958) has already thoroughly analysed the 107 histopathological reports in the literature, about one third of these fall into the classical picture of Eales's disease and two thirds were cases of retinal vasculitis undoubtedly secondary to uveitis.

These reports have shown the pathology of Eales's disease to be variable but briefly the predominant feature has been a patchy perivascular or intramural infiltration of lymphocytes (Fig. 1) or of granulation tissue occasionally with but usually without, giant cells (Fig. 2). Eosinophils have not been remarked upon, and were presumably not a feature of the reaction—a point of distinction from periarteritis nodosa. Plasma cells on the other hand, are not uncommon



FIG. 1 Retinal periphlebitis in endophthalmitis phaeo-myxomatosa. Note the marked lymphocytic infiltration around the vein while the artery is little affected. Haematoxylin and eosin.  $\times 75$ .



FIG. 2 Granulomatous reaction in a case of Eales's disease. This focus of lymphocytes, endothelial cells and a giant cell was found near a vein. P.A.S. and Haematoxylin  $\times 40$ .

considerent qu'aux neurotiques il existerait un desequilibre entre le cortex et les regions sous — corticales avec la mise en liberte des dernieres vis a vis du controle cortical celles ci en etat d'excitation augmentee, travaillent anarchiquement les ordres transmises a la peripherie dans ces conditions sont depourvus de l'action correctrice discriminatrice de l'ecorce cerebrale

Mais ces troubles generaux et les troubles oculaires — dont specialement le muscle ciliaire fatigue et epuise par ses rapides contractions continuellement repetees — beneficieront de la correction dioptrique qui est leur traitement specifique

Le but de cette correction dioptrique dans l'hypermetropie est de supplier l'amplitude de l'accommodation pour faire face au nouveau pourcentage d'hypermetropie latente devenue hypermetropie manifeste La correction de la nouvelle hypermetropie manifeste empeche la contraction du muscle ciliaire au dela de ses limites physiologiques et donc aussi la fatigue qui s'ensuit dans tous les elements oculaires ce qui en fin de compte n'excite plus anormalement le ganglion ciliaire pour declencher ses reflexes

En meme temps la correction dioptrique empeche l'incapacite du muscle ciliaire de mettre continuellement a point l'image sur la retine et par consequent empeche l'alternance des images brouillees et claires qui provoquent aussi de cette maniere un autre etat de nevrose, mais cette fois ci purement visuel

## 2 Exatement de tout autre facteur neurotique

III Les phenomenes d'incapacite adaptative retinienne seront empaches par les suivantes mesures therapeutiques

1 Preadaptation graduelle a l'obscurite avec la protection du regard envers la lumiere intense du jour par

(a) L'emploi obligatoire 20 minutes avant d'entrer dans la chambre obscure du radar de visiere protectrice a philtre de lumiere et de lunettes fumees a 75% absorption ensuite

(b) L'emploi obligatoire 30 minutes avant d'entrer dans la chambre obscure du radar — selon Platonov <sup>(1)</sup> — de lunettes rouges rubis ou l'accommodation préalable dans la chambre a la lumiere rouge

2 Desadaptation graduelle a l'obscurite — consistant de la prevention de la sensation d'eblouissement lumineux associee aux contractions — decontractions brusques du muscle ciliaire fatigue par l'effort accommodatif deploye dans la chambre obscure — par le port obligatoire de la visiere et des lunettes a philtres de lumiere apres etre sorti de la chambre obscure pendant 10-15-30 minutes, le myope gardera continuellement bien entendu comme d'habitude a la

<sup>(1)</sup> Platonov K. L'homme en vol Bucarest Ed Mil du Min des Forces Armées de la R.P.R. 1959

dont a besoin le même malade plus tard après sa guérison, lorsque le muscle ciliaire retrouve son tonus normal. C'est pour cela que les lunettes prescrites pendant la maladie sont plus fortes de + 0,50 d sph jusqu'à + 2,5 d sph, vis-à-vis des lunettes nécessaires au même organisme rétabli.

Cela explique aussi pourquoi en plein état de santé les jours où on est fatigué, les mêmes lunettes ne sont pas aussi bonnes qu'un jour où l'on n'est pas fatigué.

2 *Verres protecteurs* pour atténuer l'éclat de la lumière du soleil et de la neige, mais seulement dans les conditions indiquées plus bas (III).

3 *Position habituelle de l'observateur pendant la lecture*. Observateur en faible illumination tandis que la lumière, qui brasse le livre regardé, vient de derrière et de la gauche de l'observateur, ou de n'importe où, par l'entremise d'un abat-jour, le livre se trouvant compris dans une plume de lumière, tandis que l'observateur reste en pleine obscurité.

4 *Douche progressivement échauffée jusqu'à la limite supportable, pendant tout au plus une minute, ensuite refroidissement graduel jusqu'à la température normale, sur les yeux fermés et la face*. Ces lavages seront faits le soir, une heure au moins avant le coucher, pour que la circulation des liquides intra-oculaires ne s'aggrave pas avec le sommeil, mais continue de la sorte encore pendant quelques temps la décongestion de l'œil en général et de la musculature intra-oculaire, en particulier.

5 *Sommeil* — de préférence — naturel et suffisamment long, le relâchement le plus physiologique du muscle ciliaire, car le muscle ciliaire en général et spécialement le muscle ciliaire de l'hypermétropie ne se repose que pendant le sommeil (1).

## B MIS EN APPLICATION STRICTEMENT GÉNÉRAL

1 *Administration des tranquillisants centraux et périphériques conjointement à la correction dioptrique*. La névrose asthénopique est une maladie oculaire par sur-sollicitation visuelle à troubles ultérieurs organiques généraux, dont le reflet cortical trouble de plus encore la fonction visuelle qui aggrave les troubles généraux qui aggravent de nouveau les troubles oculaires, donc un véritable cercle vicieux qui peut être interrompu en soignant en même temps et les troubles généraux et spécialement les troubles oculaires.

Les troubles généraux, qui ne sont autre chose que des réflexes cilio-viscéraux et cilio-cortico-viscéraux à reflet viscéro-ciliaire et viscéro-cortico-ciliaire seront soignés par des tranquillisants centraux et périphériques.

D'ailleurs Bikov et Kurtin (2) qui se sont occupés des relations cortico-viscérales dans des conditions normale et pathologiques

(1) Cullmann L. Schiff Wertheimer S. Offret G. Dubois Poulsen A. Ophthalmologie. Ed Méd Flammarion 1953, p 58.

(2) Bikov K. M. Kurtin S. I. La théorie cortico-viscérale de la pathogénie de la maladie ulcéreuse. Bucarest Ed de l'Etat 1954.

Il s'agit surtout de l'incapacité du muscle ciliaire à faire face à la transformation d'un certain pourcentage d'hypermetropie latente en hypermetropie manifeste

L'oscillation tonique irrégulière du muscle ciliaire fatigué, qui, spontanément et en de très variables durées se relâche et puis reprend plus ou moins complètement son tonus normal réalise une alternance irrégulièrement brouillée et claire des images. Mais justement cette *défection informative des centres visuels est un autre mécanisme pathogénique de l'état de névrose* cette fois ci *purement visuel* qui explique très bien aussi de cette manière ci les *desordres végétatifs psychiques*

La conclusion générale sur la thérapeutique curative des troubles de la névrose asthénopique, est qu'on doit guérir la fatigue du muscle ciliaire d'abord et ensuite les troubles généraux associés non guéris par la correction dioptrique et les autres mesures thérapeutiques oculaires

Aujourd'hui les recherches de physiologie oculaire expérimentales et cliniques dévoilant les mécanismes des désordres amétropiques à participation si diverse et si importante de tout l'organisme imposent de diagnostiquer ces phénomènes

Donc pour dépister les vices de refraction qui peuvent se manifester parfois par de si graves troubles de névrose asthénopique et afin d'instituer une thérapeutique préventive une minutieuse vérification de l'état visuel devient obligatoire pour le radariste. Cela d'autant plus que ces vices de refraction muets d'habitude sont découverts soit tout à fait accidentellement soit à l'occasion des troubles visuels survenant après des efforts visuels prolongés ou à la suite d'affections générales asthénisantes

\* \* \*

À la fin de ce travail il faut ajouter que ces recherches ont pu être effectuées grâce à l'appui de l'Académicien Gr. Benetato et grâce à l'aide du Lt Colonel Al. Ionasco Chef du Service Médical de l'Aviation

Pour l'aide apportée au présent travail nous remercions chaleureusement l'ingénieur D. Bengulesco et le docteur St. Musatesco

Travail du Laboratoire de Physiologie et Physiopathologie Oculaire Clinique et Expérimentale de l'Institut de Physiologie Normale et Pathologique Danuș Drănelopolu de l'Académie de la République Populaire Roumaine

Directeur de l'Institut Académicien Prof. Dr. Gr. Benetato



lumière du jour, les lunettes de correction respective, légèrement fumées, pour la vue de loin

3 Amélioration de l'adaptation par l'alimentation riche en vitamine A, en même temps c'est évident qu'on n'admettra jamais les blonds et peau blanche, et iris de couleur claire et à fond d'œil discrètement pigmenté, donc ceux qui par leur constitution se trouvent dès le commencement au-dessous du niveau biologique exigé = un individu à réactions d'adaptation normale vis-à-vis de la lumière et de l'obscurité

IV La diminution de la capacité sexuelle déterminée par l'obscurité prolongée sera empêchée par les suivantes mesures thérapeutiques

1 La durée du travail dans la chambre obscure ne dépassera pas journalièrement 1 1/2 jusqu'à 2 heures

2 Le port de la visière protectrice et philtre de lumière et des lunettes fumées doit se réduire chez l'hypermetrope et l'emmetrope seulement à 10-15-30 minutes après l'achèvement du service, afin de réaliser une désadaptation graduelle à l'obscurité et une réadaptation graduelle à la lumière, et pas du tout au reste de la journée

3 L'exposition de l'organisme en général et de la vue en particulier à de vives « bruns de soleil »

V La protection de l'organisme vis-à-vis des ondes ultra courtes du radar sera empêchée d'une part par l'élimination des personnes et inclusions de fragments métalliques dans leur corps comme des prothèses, des projectiles, etc., et d'une autre part, bien entendu, de tous les objets métalliques, qui se trouveraient dans les poches, dans les visières, dans les montures des lunettes, etc., toutes ces inclusions métalliques aggraveront l'action des ondes ultra courtes émises par le radar (1)

VI Les conditions du micro climat de la chambre obscure du radar seront assurées par sa continuelle ventilation, et maintien constant, tant de la température fraîche que de l'humidité normale

### Conclusions sur la physiologie oculaire clinique et la thérapeutique curative et préventive de la névrose asthénopique engendrée par le radar

La conclusion générale sur la pathogénie des troubles de la névrose asthénopique, est que la fatigue du muscle ciliaire d'abord et ensuite des autres éléments oculaires qui contribuent à la perfection de l'acte visuel, incapables d'accomplir leurs fonctions, tous ces mécanismes engendrent graduellement en fin de compte d'une part, des troubles locaux oculaires et d'autre part, par l'excitation anormale du ganglion ciliaire, des troubles végétatifs dans les organes subordonnés à l'innervation ciliaire, ainsi que des troubles de l'activité corticale, qui augmentent de plus encore les troubles végétatifs

(1) Boiteau H. Les effets biologiques des ondes radar. Rev. des Corps de Santé des Armées 1960 1 5 pp 637-652

graduated superposed parallelly to the pupillar plane, and as near as possible to the eye — since the eye of the rabbit is oval having a vertical great axis — for commodity sake we have always measured its diameter horizontally

## *2° Myosis in conditions of high altitude hypobarism*

In general the rabbit was left free in the barochamber, in order to observe its general behavior and at the same time, and within possibilities, the pupillar one. However, the animal was sometimes immobilized without fastening its head, so as to follow bilaterally the pupillary modifications. Other times the rabbit was immobilized with the head secured in flexion to the right or left, resting on the transparent window of the barochamber, for measuring precisely the modifications of the pupillary diameter.

The rabbits with medicinal monolateral myosis have been subjected to very high ascents between 11 000 and 12 000 m corresponding to atmospheric pressures between 267 and 145 mm Hg. The ascent to 8 000 m, has taken 1 min 50 sec, and the return 40 sec; the ascent to 9 000 m 2 min 5 sec and the return 40 sec; the ascent to 10 000 m 2 min 24 sec and the return 44 sec; the ascent to 11 000 m 2 min 40 sec and the return 48 sec and the ascent to 12 000 m has taken 2 min 28 sec and the return to the ground 53 sec.

The most used experimental prototype has been the ascent to 9 000 m i.e. to 230 mm Hg atmospheric pressure, with a 3 min exposure at that altitude followed by the return to the ground, and a 5 min rest at normal atmospheric pressure.

A total of 52 ascents were carried out with 12 animals in a state of myosis. Sometimes the same animal in a state of myosis was subjected at the same sitting to 5 to 9 ascents while in an interval of 4 to 8 days, in another 3 sittings, to a total of 11 ascents.

The pupillary diameter was measured in a constantly luminous condition with a metallic blade millimetrically graduated pressed against the window of the barochamber and superposed parallelly upon the horizontal pupillar plane. The pupillar modifications determined by the action of high altitude hypobarism upon the rabbit in conditions of medicinal myosis have also been studied in connection with the photo motor reflex myosis caused by the 5 V focalized light of the Zeiss ophthalmoscope.

## THE RESULT OF RESEARCHES

### *1° Myosis in conditions of normal atmospheric pressure*

*1st Experiment* One drop of 1% eserine is instilled. The pupil decreases gradually from its normal horizontal slightly inconstant and around 5 mm variable diameter, to a constant horizontal diameter of

# THE MECHANISM OF THE MODIFICATIONS OF PUPILLAR DIAMETER INFLUENCED BY MYOTICS ON THE ORGANISM SUBJECTED TO HIGH ALTITUDE HYPOBARISM

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Recent experimental researches, carried out in our Institute, have shown that the eye, in general, and particularly the dynamic modifications of the iris musculature constitute a precise and delicate indicator of modifications occurring in the equilibrium of the functions of organism subjected either merely to the action of certain drugs (1) (2), or only to the action of high altitude hypobarism (3), or to the combined action of a drug (strychnine) and of hypobarism (5).

In the present investigation we propose to study the behaviour of the tonus of the iris musculature in the animal ocularly instilled with myotics, in conditions of normal atmospheric pressure and comparatively in the animal with medicinal myosis in conditions of high altitude hypobarism.

Establishing the behaviour of the pupillar diameter in these circumstances is useful for determining the action mechanism of myotics during high altitude hypobarism, and, at the same time, for eventual therapeutic suggestions which might offer valuable indications for aviation medicine.

## RESEARCH METHODS

The research was first carried out at normal atmospheric pressure, on the ground, and then at high altitude atmospheric pressure in the barochamber, for being able to appreciate correctly, and comparatively the pupillar modifications of the organism with medicinal myosis in conditions of normal atmospheric pressure, as against conditions of high altitude hypobarism.

### *1° Myosis in conditions of normal atmospheric pressure*

The action of myosis on the test animal (rabbit) has been carried out by the monocular instillation, in the right eye (O.D.), of one drop of 1% eserine and 1% pilocarpine solutions, the left eye (O.S.) serving as control.

The pupillar diameter was measured in the following way: in the rabbit placed on the observation table, always identically illuminated, the eyes exposed to an invariable luminous source, situated medially at the extremity of the nose, from below upwards, the pupillary diameter was measured with a metallic blade, millimetrically.

graduated superposed parallelly to the pupillar plane, and as near as possible to the eye — since the eye of the rabbit is oval having a vertical great axis, — for commodity sake we have always measured its diameter horizontally

## 2<sup>d</sup> *Myosis in conditions of high altitude hypobarism*

In general the rabbit was left free in the barochamber, in order to observe its general behavior and at the same time, and within possibilities, the pupillar one. However the animal was sometimes immobilized without fastening its head so as to follow bilaterally, the pupillary modifications. Other times, the rabbit was immobilized with the head secured in flexion to the right or left resting on the transparent window of the barochamber, for measuring precisely the modifications of the pupillary diameter.

The rabbits with medicinal monolateral myosis have been subjected to very high ascents between 8 000 and 12 000 m, corresponding to atmospheric pressures between 267 and 145 mm Hg. The ascent to 8 000 m has taken 1 min 50 sec, and the return 40 sec; the ascent to 9 000 m 2 min 5 sec and the return 40 sec; the ascent to 10 000 m 2 min 24 sec and the return 44 sec; the ascent to 11 000 m 2 min 40 sec, and the return 48 sec; and the ascent to 12 000 m has taken 2 min 28 sec and the return to the ground 53 sec.

The most used experimental prototype has been the ascent to 9 000 m, i.e. to 230 mm Hg atmospheric pressure, with a 3 min exposure at that altitude followed by the return to the ground and a 5 min rest at normal atmospheric pressure.

A total of 52 ascents were carried out with 12 animals in a state of myosis. Sometimes the same animal, in a state of myosis was subjected at the same sitting to 5 to 9 ascents, while in an interval of 4 to 8 days in another 3 sittings to a total of 11 ascents.

The pupillar diameter was measured in a constantly luminous condition with a metallic blade millimetrically graduated pressed against the window of the barochamber and superposed parallelly upon the horizontal pupillar plane. The pupillar modifications determined by the action of high altitude hypobarism upon the rabbit in conditions of medicinal myosis have also been studied in connection with the photo motor reflex myosis, caused by the 5 V focalized light of the Zeiss ophthalmoscope.

## THE RESULT OF RESEARCHES

### 1 *Myosis in conditions of normal atmospheric pressure*

*1st Experiment.* One drop of 1% cocaine is instilled. The pupil decreases gradually from its normal horizontal, slightly inconstant and around 5 mm. variable diameter to a constant horizontal diameter of

2 mm. Medicinal myosis sets in in 7 min. in the restful rabbit and in 10 min. in the restless one. In this situation, the reactional promptitude of the photo motor reflex myosis decreases gradually to its minimum perceptibility, which appears 15 min. after the setting in of the respective maximum myosis produced in 7 or 10 min., after this, the inducing of the photo motor reflex myosis diminishes the pupil to a 1 mm. diameter, while the interruption of the luminous stimulus brings the pupil immediately back to the previous 2 mm. diameter.

*2d Experiment* One drop of 1% pilocarpine is instilled monocularly. The pupil is gradually reduced from its normal, horizontal diameter, slightly inconstant and variable around 5 mm., to a constant and invariable, horizontal diameter of 1 mm. Medicinal myosis sets in in 7 min. in the restful rabbit, and in 10 min. in the restless one. In this situation, the reactional promptitude of the photo motor reflex myosis diminishes gradually to its minimum perceptibility, which appears after 26 min. from the setting in of the respective maximum myosis, produced in 7 or 10 min., thereafter, the inducing of the photo motor reflex myosis diminishes the pupil to a 3 mm. diameter, while the interruption of the luminous excitation brings the pupil immediately back to the previous diameter of 4 mm.

*A B* In both experiments, the pupil of the opposite eye reacts, all this time, normally. Thus, its normal horizontal diameter, slightly inconstant and variable around 5 mm., is modified simultaneously with the inducing of the photo motor reflex myosis, to a horizontal, inconstant diameter, varying around 4 mm. The interruption of the luminous excitation brings the pupil immediately back to its normal, slightly inconstant diameter, varying around 5 mm.

## 2° *Myosis in conditions of high altitude hypobarism*

The researches carried out in conditions of fictitious high altitude hypobarism in the barochamber, with a monolateral instillation of 1-2 drops of 1% eserine and pilocarpine solutions, have yielded the following results:

1 The 2 mm. eserinic myosis is transiently reversible during the more or less accentuated convulsions of the animal, thus, while the pupil of the non instilled eye (O S) was in a maximum 9 mm. mydriasis, the pupil of the instilled eye (O D) had 6 mm., when the O S pupil had 8 mm., the O D pupil had 5 mm., when the O S pupil had 7 mm., the O D had 4 mm., and when the O S pupil had 6 mm., the O D had 3 mm. Thus, the relations between the dimensions of the pupils, when starting from the ground — O S 5 mm., O D 2 mm. — remains unaltered during the subsequent increase in their diameter, maintaining themselves constantly by 3 mm. smaller in the instilled eye as against the non instilled one.

2 The 4 mm. pilocarpine myosis is likewise transiently reversible during the more or less accentuated convulsions of the animal, thus, when the pupil of the non instilled eye (O S) was in a 9 mm.

maximum mydriasis the pupil of the instilled eye (O D) had 8 mm, when the O S pupil was in a 7-8 mm medium mydriasis, the O D pupil had 6-7 mm, and when the O S pupil was in a light mydriasis of 6 mm, the O D had 5 mm. Thus the relation between the dimensions of the pupils when starting from the ground — O S 5 mm, and O D 4 mm — remains unaltered during the subsequent increase in their diameter, maintaining themselves constantly with 1 mm smaller in the instilled eye as against the non instilled one

3 Medicinal myosis are modified the more rapidly, the more the number of ascents grows, which induce convulsions and finally bring about only generalized muscular quiverings

4 The action of hypobarism, preceding by several minutes the effect of the myotic delays the appearance of myosis in proportion to the altitude to which the animal had been raised

5 The photo-irido motor reflex is absent during maximum mydriasis much delayed during medium mydriasis and slightly delayed in the case of discreet mydriasis in the non instilled eye. In the instilled eye however, indifferently of the dimension of the pupil it appears after a long period of latency and is very discreet

## INTERPRETATION OF RESEARCHES

### 1 *Myosis in conditions of normal atmospheric pressure*

By the inactivation of local cholinesterase and the local favouring of the action of acetylcholine eserine and pilocarpine induces the myosis of the eye on which they had been instilled

The pupillary phenomenon of the parasympathetic type of these two myotic drugs thus set in by the intermediary of a similar action mechanism which is however not identical by the intensity of its manifestation since eserine myosis is more accentuated than the pilocarpine one hence the inference that the favouring of the acetylcholine action is weaker in the case of pilocarpine than in that of eserine

Medicinal myosis occurs more slowly in the restless agitated animal than in the restful, calm one. This because the restless animal is in a state of central excitation which has a stimulating effect upon the medullo suprarenal hence the local favouring of the acetylcholine action consequent on the inactivation of cholinesterase, induced by the myotic will be delayed by the transient and repeated action of adrenaline which not only acted upon organism previous to instillation but operates even during the action of the instilled drug and which consists on the one hand in the diminution of the reactivity of the iris cell towards the parasympathomimetic action of acetylcholine and on the other in the freeing of the sympathomimetic reactivation towards the local sympathum. In the calm animal however, in which the acetylcholine generating state of central excita-

tion is lacking, it is evident that the action of the myotic will no longer be delayed.

If we equate the state of central excitation of the animal which incites its uneasiness, with the state of man's central excitation of a completely special type, which might bring about glaucoma, the above state of facts might thus justify the delayed effect of myotics upon glaucomatous mydriasis. In this case the particularly important therapeutic conclusion is that — as shown in the researches of some of us (3), — in the patient's agitated days, myotics cannot fulfill, in ophthalmological clinic, the expected effect, because of the plainly predominant effect of the action of adrenaline upon the action of acetylcholine, insufficiently favoured by myotics. Therefore, in the very same glaucomatous patient, at the same stage of the complaint, the intraocular action of the myotics varies with the general nervous state of the patient, i.e. this action is exercised in a curative sense in periods of calm and in a quasi curative or completely non curative sense in the patient's periods of agitation, hence the imperative necessity to associate to the treatment with myotic instillations, that of a general sedative drug.

As a matter of fact, Soviet researches come to the support of the conception that adrenaline enters the physiopathological circuit of glaucoma, bringing unquestionable biochemical evidence regarding the *sympathetic predominance* of the disturbance of the sympathetic — parasympathetic equilibrium of the nervous vegetative system in glaucomatous persons. Thus Popov's researches (quoted at (6)) have underlined the increase in Cr and adrenaline, and the decrease in A, I and choline in the blood of most glaucomatous patients. While Platnev, Rabin and Voronin (quoted at (6)), examining, by Levy's method, the aqueous humour of glaucomatous persons, have emphasized the usual presence of the chemical adrenaline sympathetic mediator which raises the activity of the heart and much more seldom that of the vagotrophic substance, the acetylcholine, which lowers the activity of the heart.

The irido motor reflex consists in the constant reduction of the respective pupillary diameter surprised with 1 mm, under the influence of the luminous excitant (eserine 2 mm — 1 mm = 1 mm, pilocarpine 4 mm — 1 mm = 3 mm).

The photo motor myosis or the irido photo motor reflex reaches its minimum perceptibility a very long time after the setting in of the medicinal myosis, namely 45 min. after the setting in of eserine myosis and 26 min. after that of pilocarpine myosis, which permits the establishing of a directly proportional relation between the intensity of medicinal myosis, undoubtedly connected with the intensity of the local favouring of the action of acetylcholine and the time passed up to the minimum perceptibility in this state of photo motor myosis, i.e. the more accentuated the medicinal myosis becomes, the longer it takes for the photo irido motor reflex to reach its minimum perceptibility.

The veins are particularly affected, although arteries and capillaries are not immune, and characteristically the vasculitis begins at the periphery and may extend backwards even as far as the optic nerve and intracranial vessels (Safar, 1928, Ballantyne and Michaelson, 1937, Verhoeff and Simpson, 1940, Lowenstein and others, 1946) but sometimes the vasculitis may start posteriorly and spread to the periphery. Vasculitis thus appears to be the primary change while the capillary irregularities of beading and microaneurysm formation, the recurrent retinal haemorrhages, retinitis proliferans (Fig 3), retinal detachment, glaucoma etc, are all secondary and apparently



FIG 3 Lales's disease showing new vessels extending into the vitreous from the peripheral retina. Haematoxylin and eosin  $\times 112$

non specific developments. Dodon (1960) believes, however, that exudative, proliferative and haemorrhagic forms are clinically quite distinct.

A granulomatous reaction is far less frequent than a non specific lymphocytic cuffing. In the series reported by Kimura, Carricker and Hogan (1956) twelve eyes showed vasculitis confined to the retinal vessels and in only four of these was the reaction granulomatous. In a case of my own, a male aged 40 years with typical Lales's disease the sections showed a patchy granulomatous perivasculitis with giant cells and macrophages, but no causative agent was found (Fig 2).

As already mentioned, an inflammatory reaction may be entirely absent. In one interesting case reported by Elliot (1954) (a 21 year old male with typical Lales's disease who died from tuberculous pericarditis only six months after the onset of the eye condition) pathological examination of the eyes revealed no inflammatory process around the vessels, which showed only hyaline thickening. Elliot came to the conclusion that these findings were compatible with the theory that the disease had an allergic basis, but it is surprising that the inflammatory reaction disappeared so rapidly.



## 2° Myosis in conditions of high altitude hypobarism

On the ground the local favouring of the action of the acetylcholine by the instilled myotic has a constant character throughout the latter's action

In the barochamber in conditions of high altitude hypobarism, however the respective 2 mm. *eserine*, and the 4 mm pilocarpine myosis are transiently reversible and only for the duration of the convulsions of the animal

Thus means that the local favouring of the acetylcholine action by the instilled myotic is subsequently surpassed by the general transitory favouring of the action of adrenaline, subsequent to the passing suprarenalian excitation either directly by anoxious hyperadrenabnaemia or indirectly by the increased reactivity to acetylcholine of the higher nervous centres under the influence of hypobarism, whence an important flood of adrenaline, which justifies the maximum mydriasis of the non instilled eye and concomitantly meanwhile the tendency of the pupil to return to normal or even the normalization of the pupillary diameter of the instilled eye. Thus the fleeting mydriasis of the non instilled eye, always synchronous with the proportional increase in the pupillar diameter of the instilled eye are phenomena occurring during convulsions determined by hypobarism which by the general favouring of adrenaline hyperproduction mechanisms, act locally upon the iris cell on the one hand, by the diminution of the reactivity of this cell towards the parasympathomimetic action of local acetylcholine — favoured by the instilled myotic — and on the other hand by the freeing of the reactivity of the same cell towards the sympathomimetic action of local sympathin

Thus the degree of spontaneous adrenaline mydriasis points out the directly proportional intensity of the degree of the general favouring of the adrenaline hyperproduction mechanisms which act upon the iris in the conditions of the latter's reactivity. In other words the iris not influenced by any instilled drug will always react strictly, proportionally to the quantity of adrenaline which will arrive on the eyeball. But what happens if the reactivity of the iris is influenced by the local parasympathomimetic action of acetylcholine favoured by the instilled myotic and still more so in the case of *eserine* than in that of pilocarpine? Then starting from this state of reactivity, the pupillary diameter a result of the two actions ( $DPR$ ), — the diminution of the iris reactivity towards the parasympathomimetic action of local acetylcholine ( $Rip$ ) favoured by the respective instilled myotic and the liberation of the iris reactivity towards the sympathomimetic action of adrenaline arrived on the eyeball ( $Ris$ ) — will manifest itself by the increase in the diameter of the pupil in medicinal myosis to a new pupillary diameter resulting ( $DPR$ ) from the pupillary difference ( $DifP$ ) between the diameter of the normal pupil ( $Dpn$ ) and the one influenced by the myotic ( $Dpmo$ ) a pupillary difference ( $DifP$ ) then deducted from the pupillary diameter of the

non instilled eye, mydriatized (D P mid) by hypobarism. This situation may be formulated as follows

$DPR = R_{ip} - R_{is}$ , namely

$Dif P = DP_n - DP_{nuo}$ , while

$Dif P - DP_{mid} = DPR$ , for instance in eserine

$Dif P (3 \text{ mm}) = DP_n (5 \text{ mm}) - DP_{nuo} (2 \text{ mm})$

$Dif P (3 \text{ mm}) - DP_{mid} (9, 8, 7, 6 \text{ mm}) = DPR (6, 5, 4, 3 \text{ mm})$  pilocarpine

$Dif P (1 \text{ mm}) = DP_n (5 \text{ mm}) - DP_{nuo} (4 \text{ mm})$

$Dif P (1 \text{ mm}) - DP_{mid} (9, 8, 7, 6 \text{ mm}) = DPR (8, 7, 6, 5 \text{ mm})$

In this case, one may speak of the  $R_{ip}$  intensity directly connected to the respective myotic, since the subsequent pupillary modifications under the adrelinogenous influence of hypobarism occur from this reactional level

The same adrelinogenous influence of hypobarism explains the delay in the action of the myotic, exercised synchronically with the conditions of high altitude

The photoirido motor reflex of the instilled and non instilled eye, manifests itself in relation both with the intensity of the surprised iris contraction, as well as with the type of predominant iris contraction, either parasympathetically, agonistic in the first case, or sympathetically antagonistic in the second case, therefore in the instilled eye the reflex manifests itself very discreetly and only after a long period of latency, while in the non instilled eye, the reflex which is abolished in maximum adrenaline mydriasis manifests itself much delayed in medium mydriasis, and slightly delayed in discreet mydriasis

## CONCLUSIONS

Eserine myosis is more intensive than the pilocarpine, since the favouring of the acetylcholinic action is stronger in the case of eserine than in the case of pilocarpine

Myosis appears slower in the restless animal than in the restful one, a fact which signifies that the first is in a state of central excitation, which has a stimulating effect upon the suprarenal glands, while the second, not being in a state of central excitation, thus not stimulating the suprarenal glands to liberate adrenaline, the favouring of the acetylcholinic action of the myotic is no longer delayed

The irido photo motor reflex always diminishes by 1 mm both the normal pupil and the pupil in the respective medicinal myosis hence the significance that the iris excitability threshold is unchanged towards luminous excitation

The fact that irido photo motor myosis reaches its minimum perceptibility a very long time from the complete setting in of myosis

shows that this very long time must elapse from the setting in of medicinal myosis until the final functional influencing of the iris cell by the action of the myotic

In conditions of high altitude hypobarism, the general favouring of the mechanisms of adrenaline hyperproduction takes place, which, at the level of the eyeball, liberating the iris reactivity towards the sympathomimetic action of adrenaline, modifies the medicinal myosis. The increase in the pupillary diameter in medicinal myosis, represents, therefore, the resultant of the two local actions: the parasympathetic and the sympathetic, in which the latter, favoured by adrenaline predominate, but the parasympathetic action hinders, all the same, a mydriasis identical with the one of the non instilled eye therefore without any parasympathetic favouring and in which pupillary modification will be the sole result of sympathetic favouring.

Adrenalinogenous acting of hypobarism justifies on the one hand, the delay in the action of the myotic instilled simultaneously with the subjection of the animal to conditions of high altitude.

The irido photo motor reflex depends in its manifestation both on the intensity of the surprised irian contracture, and on the predominant iris contraction time, either agonistically or antagonistically to the photo motor myosis.

The Laboratory for Clinical and Experimental Physiology and Physiopathology of the Eye of the Normal and Pathological Physiology Institute Daniel Danelopolu of the Academy of the Rumanian People's Republic Director of the Institute Academician Prof Dr Gr Benetato

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**SYMPOSIUM V**  
**CLINICAL ELECTRORETINOGRAPHY**



# FREQUENCY ANALYSIS OF THE ELECTRORETINOGRAM\*

(A preliminary report)

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When we are faced with an electroretinogram (ERG) we are accustomed to measure amplitude, to look for polarity, whether there is an a, b or x wave, wavelets or an off effect. Perhaps we measure latency and other times. We were not too much interested in frequency till now and that is also an essential characteristic of an electric potential.

We started our investigations at first only to know, what the frequency range of the apparatus must be, to get an undisturbed ERG. The results of this work we will publish in another paper. In this connection it is only of interest that a low frequency filter pass which cuts down all frequencies over 200 cps, has no visible influence on the LRG.

Afterwards we became really interested, which frequencies it are which build up the ERG. Therefore we tried to make a frequency analysis. Many of you when they hear frequency analysis will think at the work of GRANIT and WIRTH and HENKES and coworkers, who used frequency analysis in connection with flicker. Our problem is quite another one. We want to know, which frequencies are in a single LRG.

One can do a mathematical frequency analysis or a physical one. With single curves mathematical frequency analysis is rather difficult especially the first part of the curve is not to analyse as far as I know. We choose an electric way for analysis. For that purpose it is necessary to reproduce the same LRG many times and therefore one has to store it. One can store such a potential continuous—that is the analogue method for example with a tape recorder or one can do it in steps—that is the digital method for example with the most computers. The latter method is used by JACOBSON and TAKASHI. The computer has the advantage that the possibilities for disturbances of the curve are more or less because it works only with on off responses. On the other hand there are always steps and there must be many steps to get a result as continuous like with an analogue method.

We registered the ERG on a tape recorder. That is rather difficult to do. Some of you will know that a sufficient direct transformation

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\*This work was supported by a grant from Deutsche Forschungsgemeinschaft





The frequencies in the ERG seem to be a special harmonic row. Perhaps that means, that the high intensity ERG is an overloaded system and therefore there are harmonics. One has to bear in mind, that our analysis deals with the ERG we register and there is no simple conclusion to that, what originates in the retina.

We wanted to give only a preliminary report. Before saying more we need more experiments.

99 0 1 2 3 4

100 2

65 2

32 2

16 2

16 32 64

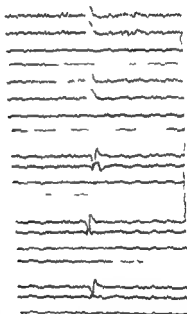


Fig. 1. High Intensity ERG (white light 10 000 ash visual field 110) in dark adapted human eye. In the figure records the upper beam is for comparison in the lower beam the special frequency is suppressed. For further explanation see text.

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of slow potential changes on a type recorder is technically impossible. One has to modulate the ERG on a carrier frequency. This modulation can be a frequency modulation or an amplitude modulation. Arrington and coworkers used for their investigation frequency modulation and it may well be, that is the better way, in the meantime there exist several commercial type recorders, which work with frequency modulation. We ourselves used amplitude modulation. At first we were rather disappointed to see what came out. Little inhomogeneities and failures in the magnetic film of the tape caused what is called "drop outs". These drop outs modulate the carrier frequency in the same manner like the signal and disturb the curve seriously. We tried many ways and finally we are rather content now. We go direct coupled with push pull through our whole apparatus. That means we give two modulated carriers in our type recorder and the drop outs compensate each other. The upper limit of frequency range of our whole apparatus is 330 cps. This is well over the limit of frequency range, which is necessary to get an undisturbed LRG.

With the frequency analysis we started only in the last time. We used phase shift amplifiers working with RC networks and Wien bridges with a negative feed back. Unfortunately our most filters were at the input condenser coupled. So we have a lack in our analysis for the lowest frequencies. With 5 cps we had a loss of 50%, with 7 cps of 30%. We are on the way to change that.

Until now we have analysed only one state of LRG. We choose a high intensity ERG of the dark adapted human eye. Now to the result. We have the impression, that there are some frequencies, which dominate in the ERG. In figure 1 these dominating frequencies are suppressed. Our filters are not so small, that we can suppress only one frequency and the neighbourhood is in no way altered. Therefore we can only say, that we found minimums with that special frequencies. But from the many pictures we saw, when we played with our filters and the ERG we had the strong impression, that there are single dominating sinus waves. The figure shows five records. In the lower three ones we used in addition to the special suppressed frequency a low frequency filter pass with an upper limit of about 50 cps. We did that, because in these records we were not interested in the higher frequencies. The upper beam shows always an ERG for comparison and in the lower beam the special frequency is suppressed. The third beam is for time and photocell registration but that is one of our child diseases, it did not work well.

When the frequency of 128 cps is suppressed there are no more wavelets. With 64 cps also something happens. The curve flattens a little and perhaps therefore some of the wavelets are better to see, than in the original curve. The frequencies, which seem to be the most prominent, are 32 and 16. But we should not forget, that these filters are condenser coupled and therefore there is a lack in the low frequencies. We had the impression, that between 7 and 10 there is a frequency, which has some influence and there may be lower ones too.

Other changes to be found in Eales's disease are a marked thickening of the inner limiting membrane (Guyton and Reese, 1948), which was very pronounced in one of my own cases (Fig 4), retinal gliosis,



FIG 4 Peripheral retina from a case of Eales's disease. Note the extreme thickening of the internal limiting membrane and the haemorrhages into the vitreous. Mallory triple stain  $\times 112$ .

and capillary obliteration as may be seen in injected specimens (Fig 5) which occurs especially in those areas where the intravitreal new vessels form (Fig 6) being stimulated by the local anoxia rather than the haemorrhages (Ashton 1957). There may be organising thrombi in the retinal veins which may subsequently disappear entirely in a fibrotic gliosing scar and occasionally the endothelial cells of the vessels may proliferate into the lumen as also occurs in venous thrombosis generally (Fig 7) (Hamura et al 1956). The pronounced hyaline thickening of the vessels is well seen in cross sections and pigment containing macrophages often surround them in sharply localised areas (Fig 8).



FIG 5 Eales's disease. Peripheral retina showing extensive capillary obliteration and beading of the patent vessels. Injected Indian ink  $\times 35$ .



FIG 6 Eales's disease showing peripheral neovascularization. Note that it arises in an area of capillary obliteration. Injected Indian ink  $\times 18$ .



FIG 7 Endothelial proliferation in a retinal vein in a case of central venous thrombosis. Haematoxylin and eosin  $\times 190$ .

The frequencies in the ERG seem to be a special harmonic row. Perhaps that means that the high intensity ERG is an overloaded system and therefore there are harmonics. One has to bear in mind, that our analysis deals with the PRG we register and there is no simple conclusion to that what originates in the retina.

We wanted to give only a preliminary report. Before saying more we need more experiments.

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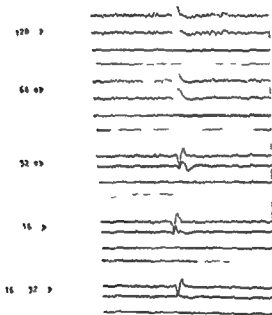


FIG 1 High Intensity ERG ( white light 10 000 asb visual field 110 ) in dark adapted human eye. In the five records the upper beam is for comparison in the lower beam the special frequency is suppressed. For further explanation see text.

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# CHANGEMENTS ELECTRORETINOGRAPHIQUES A L'ETAT HYPNOTIQUE

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## I

Dans l'étude de l'hypnose comme phénomène physiologique il y a une forte tendance d'étudier ce problème par des méthodes expérimentales objectives. Nous nous sommes mis comme devoir partiel d'examiner l'influence des changements fonctionnels du système nerveux central pendant l'hypnose sur les faits bioélectriques dans la périphérie de l'analyseur visuel dans la rétine.

La personne examinée était adaptée pendant 5 minutes à une illumination de 25 lx. Le stimulateur était un éclair électronique à une période de stimulation de 0,002 seconde et peu près. Nous avons répété régulièrement les stimulus lumineux toujours après 15,20, éventuellement 30 secondes. Nous avons fait chaque fois une série d'ERG photopiques au cours de l'hypnose et après le réveil. Nous avons ainsi établi 11 séries d'ERG dans 7 personnes âgées de 24 à 48 ans. Avant l'hypnose nous avons fait 171 ERG évaluables, pendant l'hypnose 167 et après le réveil 113 ERG. Afin d'empêcher la paupière supérieure de tomber pendant l'hypnose, nous avons appliqué à l'œil droit un blepharostat pour assurer ainsi qu'une quantité constante de lumière tombe sur la rétine. L'œil gauche était sans blepharostat et d'après l'abus de la paupière supérieure nous avons évalué le début de l'hypnose.

L'hypnose était provoquée par suggestion verbale, pour la fixation visuelle nous nous sommes servi des contours de la lampe du photostimulateur. Nous avons choisi pour l'examen des personnes qui étaient déjà auparavant hypnotisées et entrèrent facilement dans l'état hypnotique moyen, l'hypnotisme. Les personnes examinées appartenaient du point de vue diagnostique dans le groupe de névroses, éventuellement des personnalités psychopathiques avec des difficultés neurotiques.

## II

Les changements dans ERG au cours de l'hypnose étaient de terminés sur des séries d'ERG dans deux personnes sur les paramètres suivants

- 1 Une diminution du potentiel de l'onde a
- 2 Une augmentation ou diminution du potentiel d l'onde b
- 3 Prolongement du temps du parcours de l'onde b

Dans les autres 5 personnes les constatations de l'ERG au cours de l'hypnose étaient moins exprimées ou ne pouvaient pas être prouvées statistiquement. Dans ces personnes examinées on n'arrivait pas à un degré d'hypnose aussi grand que dans des personnes dont les constatations étaient statistiquement changées.

## III

La plupart des chercheurs dans le domaine de l'hypnose considèrent l'état hypnotique comme un fait du centre nerveux. Aussi dans l'analyseur visuel la suppression hypnotique se fait surtout dans les régions centrales. Chez les personnes examinées avec une constatation positive une interruption du contact visuel avec les environs a eu lieu. Ils disaient que parfois ils ne concevaient pas les éclairs répétés de la lumière. Dans la littérature sont décrits des troubles de vue pendant l'hypnose qui se produisaient spontanément sans suggestion spéciale (Doellken). En 1956 Vanysek s'occupait des rapports entre le système nerveux central et l'adaptation de la rétine au crépuscule que se traduisait sur l'électroretinogramme par une baisse de l'onde a après une suggestion verbale de l'imagination d'un éblouissement. La question d'un reflet centrifuge des fonctions centrales dans la périphérie de l'analyseur intéressait déjà I. M. Setchenoff qui maintenait que la perception est un enchaînement réflexeur compliqué. L. N. Sokolov juge qu'en dehors de la fonction centripétale au cours de la perception généralement admise existe aussi un fait contraire passant du centre vers la périphérie. Il s'agit ici d'un complément réversible. L'auteur régulation dont un exemple est la photoréaction des pupilles influence du centre sur la formation du pourpre visuel et autres.

Kozousek et Vanysek présument à la base des études antérieures que dans le rapport de la rétine avec la partie centrale de l'analyseur il existe trois types basaux de la régulation déjà connus dans les sciences naturelles. Ils peuvent être exprimés par des formules et des connexions schématiques. Le plus bas degré est la régulation proportionnelle le plus haut degré la régulation dérivative et intégrale. Dans la rétine se font valoir tous les trois sortes de régulation. Les centres cérébraux régissent le complément réversible qui se fait valoir directement dans la rétine.



## CONCLUSION

Les constatations que nous venons d'exposer montrent que l'état inhibiteur du cerveau peut avoir une influence considérable sur le cours de potentiels de la rétine qui peut être considérée comme une autre preuve de l'activité régulatoire du fonctionnement cérébral sur le fonctionnement de la rétine.

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[illegible]

All patients of the group receiving cystein (electrophoresis 3-5 per cent solution) have displayed temporary increase of visual function

In four patients FRG appeared immediately after the administration of cystein and gradual further abolishment of ERG

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## ON THE REGISTRATION OF ELECTRICAL PROCESSES IN THE ISOLATED RETINA AND THE OPTIC NERVE IN COLD BLOODED ANIMALS MAMMALS AND MAN

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VATSKAYA L D and MIRZA AVAKIAN I I (USSR)

The investigations of the Physiological Institute of the University of Leipzig have shown that the isolated retina washed in the cultural solution (modified Tirode Solution or Plasma) can be used for the study of the role of metabolic processes in the generation of the ERG

In the paper of W Sickel and G Demurtchoghian (1961) the role of the Sff groups in the origin of the ERG of the frog has been shown and the ERG of the isolated retina of man was recorded

In our laboratory investigations have been made on the study of the light and dark adapted isolated frog retina and optic nerve. The off effect of the total discharge of the optic nerve increased significantly and the on effect decreased after the light adaptation. This could be repeated many times provided the preparation is in a good functional state (the preparation has been active during two days)

In mammals enucleation of the eye and a part of the optic nerve has also been performed. The isolated retina and the optic nerve were washed with a warm plasma. The electrical reaction has been recorded by microelectrodes and cathode ray oscillograph with a d c amplifier. The FRG and the electrical activity of the optic nerve were recorded during 3-4 hours. Various chemical effects of substances used in ophthalmology were also studied.

In three patients the eye was enucleated and the ERG of the isolated retina was recorded after washing with a warm and fresh plasma during 4-6 hours. The FRG consisted of the a and b waves the d wave was absent.

The microelectrode recording permitted us to discover the FRG of the different layers of the isolated retina of man.

# THE MOLECULAR BASIS OF THE ORIGIN OF THE ERG OF ANIMALS AND MAN

DELMIRTCHOGHIAN, G. G. (USSR)

In our investigations great attention has been paid to the determination of the role of SH groups of light sensitivity and other protein substances of the retina in primary visual processes and ERG in the normal and other pathological states.

The important role of the SH groups in the nature of primary visual processes and the metastable state of light-sensitive molecules served as an initial theoretical assumption (Demirtchoghian, 1950).

The importance of the SH groups in the development of photochemical processes in rhodopsin was shown, as it is known (Wald & Brown, 1951).

Later, it was shown in our laboratory that the change of retinal function (ERG) after the action of ionized radiation may be connected with the decrease of the amount of SH groups in the retinal homogenates (Ohanjanyan, V. G., 1959).

More direct information has been received on the role of the SH groups in the origin of ERG at the Physiological Institute of Leipzig (W. Sickel and G. Demirtchoghian, 1961).

The preparation isolated from the retina of the frog, man, or man was placed in a chamber with electrodes and washed by a cultural solution (modified Tyrode solution or plasma), the addition of mercury containing substances (uracil  $10^{-6}$  or  $10^{-5}$  M) has led to the rapid extinction of the ERG. Light adapted retina was more sensitive to the blockade of SH group than the dark adapted one.

After adding cysteine ( $10^{-4}$  or  $10^{-5}$  M) to the cultural medium the complete recovery of ERG and its spectral sensitivity was obtained. Cysteine has also shown protective effect when the SH group of the retina was blocked.

In experiments of the normal isolated retina of man it was discovered that by adding uracil ( $10^{-5}$  M) to the plasma no effect of ERG extinction was noticed. The action of cysteine had little effect ( $10^{-4}$  M).

From the data received and the capability of cysteine to preserve the retina of the rabbit from the development of pigment degeneration (Sorsby and Harding, 1960) experiments were made on the study of cysteine action on the retina of patients with retinitis pigmentosa (G. G. Demirtchoghian, I. Blazutskiy, J. Mirza Aliyev, S. Gevorgyan, 1961).

detecting at a clinically benign stage those cases which will go on to malignant stage and carry a distinctly poorer prognosis before retinopathy has become clinically apparent or gross biochemical changes in blood have taken place

It is surprising that with so much of fundamental background known to the physicians the physiologists and the ophthalmologists and so much of clinical material abundantly available in all clinics the utility of electro retinography has not been adequately exploited in the assessment of prognosis in Systemic Vascular Hypertension

This report is based on a study of 96 cases of essential hypertension 63 of which could be followed up for upto 2 years after the first record. In the control series of comparable age groups the average b potential was 0.30 mV the response was sub normal in 29% and normal or super normal in 71% cases. A response of 25 to 35 mV is therefore considered a normal range. Potential below 25 mV is treated as sub normal and above 35 mV as super normal.

It should however be made clear that FRG records of this study are qualitative in nature and not of quantitative accuracy. It is based on electro retinography by Harpes initial method with five minutes dark adaptation, 80 lux illumination stimulus of  $\frac{1}{2}$  sec repeated at 15 sec interval and the potential recorded on an electro cardiograph with an amplification of 1 mV on 1 cm. It can therefore at best be expected that these observations open out a field of more intricate studies in clinics where more advanced and sensitive electronic equipment facilities are available.

Hypertensive cases were mostly in the age group of 30 to 70 years and only 7 cases were between 18 to 25 years and five older than 70 years.

The following table I summarises the electrical response of the retina in relation to the grade of retinopathy and average blood pressure.

TABLE I

Grade of Retinopathy	No of Cases	Average Blood pressure	Average b-potential			
			Normal or Super normal		Sub normal or Extinguished	
			%	°	%	°
Grade I	6	16.109	12	43.0°	14	57.0°
Grade II	33	190/174	16	48.5°	17	51.5°
Grade III	18	217/123	8	44.5°	10	55.5°
Grade IV	19	223/134	5	26.3°	14	74.7°

# ELECTRO RETINOGRAPHY IN SYSTEMIC VASCULAR HYPERTENSION

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Not foreseeing the future victims of radiation, 30% of deaths after the adult age are of vascular origin whether cardio-vascular, cerebrovascular or vasculo vascular. Whether as a consequence or as a basic cause, clinical hypertension is a subject attracting more and more attention. Therefore every medical consultant is interested in being able to pre judge the further progress and prognosis of an individual case. There are cases who have lived a full span of life consistent with hypertension while there are numerous others who though start as innocuously have their fate sealed within a few months to a few years. Efforts at assessing a prognosis are still limited to blood bio chemistry and grading of retinopathy. If a person's blood urea is markedly raised and his retinopathy is in grade IV, no insurance company will cover him as a risk, and the journey before the patient is so short and fast that hardly can he think and plan.

After all, every case of hypertension starts as a simple case and it is therefore pertinent that one would if possible like to sort out hypertension at a much earlier stage and to decide as to which particular case is likely to go on to malignancy and which particular case will be compatible with full span of life.

Retinal function is directly dependant upon the vascular nutrition it receives. Any metabolic or nutritional disturbance is likely to be manifest as a functional deficiency even though it may be sub clinical. Good visual acuity, full field of vision and normal ophthalmoscopic findings are consistent with a retina which may be functioning under certain handicap for example Vitamin A content of plasma must fall from a normal level of 98 to 192 I.U. to as low as 30 international unit/100 c.c. before clinical night blindness may become manifest.

Blood circulation in the eye being of the decisive importance for the type and shape of electro retinogram, systemic vascular hypertension associated with arterial attenuation and consequent subclinical anemic condition of retina may result even though clinically and anatomically structures appear normal. It should therefore, be a live possibility that electro retinographic studies in hypertension may possibly help in

The veins are particularly affected, although arteries and capillaries are not immune, and characteristically the vasculitis begins at the periphery and may extend backwards even as far as the optic nerve and intracranial vessels (Safar, 1928, Ballantyne and Michaelson, 1937, Verhoeff and Simpson, 1940, Lowenstein and others, 1946) but sometimes the vasculitis may start posteriorly and spread to the periphery. Vasculitis thus appears to be the primary change while the capillary irregularities of beading and microaneurysm formation, the recurrent retinal haemorrhages, retinitis proliferans (Fig 3), retinal detachment, glaucoma etc., are all secondary and apparently



FIG 3 Eales's disease showing new vessels extending into the vitreous from the peripheral retina. Haematoxylin and eosin  $\times 112$

non specific developments. Doden (1960) believes, however, that exudative, proliferative and haemorrhagic forms are clinically quite distinct.

A granulomatous reaction is far less frequent than a non specific lymphocytic cuffing. In the series reported by Hamury, Carricker and Hogan (1956) twelve eyes showed vasculitis confined to the retinal vessels and in only four of these was the reaction granulomatous. In a case of my own, a male aged 40 years with typical Eales's disease the sections showed a patchy granulomatous perivasculitis with giant cells and macrophages, but no causative agent was found (Fig 2).

As already mentioned, an inflammatory reaction may be entirely absent. In one interesting case reported by Elliot (1954) (a 24 year old male with typical Eales's disease who died from tuberculous pericarditis only six months after the onset of the eye condition) pathological examination of the eyes revealed no inflammatory process around the vessels, which showed only hyaline thickening. Elliot came to the conclusion that these findings were compatible with the theory that the disease had an allergic basis, but it is surprising that the inflammatory reaction disappeared so rapidly.

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Grade III	18	217/123	8	44.5°	10	55.5°
Grade IV	19	223/134	5	26.3°	14	74.7°

It will be appreciated from this table that 51.5 to 57% cases have a sub normal LRG which is distinctly higher than the normal percentage. It is however still significant to note that the percentage of sub normal response suddenly increased to 74.7% in grade IV retinopathy. It will also be noted that this increase in subnormal response is also proportionate to the increase in blood pressure. It is therefore suggested that the electrical retinal potential may have a direct relationship to the grade of retinopathy and the severity of hypertension.

Again table II below correlates the retinal response to systolic, diastolic and pulse pressure.

TABLE II

		No of cases	Normal or Super normal		Sub-normal or Extinguished	
			No	%	No	%
Systolic	150-199	47	24	53.2%	23	46.8%
	200-250	40	14	35.0%	26	65.0%
	Over 250	9	2	22.5%	7	77.5%
Diastolic	95-124	62	26	42.0%	36	58.0%
	125-150	29	12	41.4%	17	58.6%
	Over 150	5	1	20.0%	4	80.0%
Pulse Pressure	30-74	48	25	52.0%	23	48.0%
	75-100	34	12	35.3%	22	64.7%
	Over 100	14	3	21.5%	11	78.5%

It is again significant to note that the percentage of sub normal response is directly proportional to the increase in systolic, diastolic and pulse pressure.

In the same way the following table III is an attempt of correlating the b potential to the prognosis of hypertension.

TABLE III — Follow-up in Relation to b Potential

	No of Cases	Super normal or normal		Sub normal or Extinguished	
		No	%	No	%
Improved	28	15	53.5%	13	64.5%
No Improvement	15	5	33.3%	10	66.6%
Died	20	6	30.0%	14	70.0%



These observations equally strictly support the earlier suggestion in a follow up of 63 cases which could be dependably followed up for 2 years. Of 28, which continued to improve with treatment only 46.5% had a subnormal response. 66.0% were subnormal in those 15 which did not respond to therapy. The percentage of subnormal response was 70.0% in those 20 cases who later died within 2 years of the follow up period. A subnormal response thus is again suggestive of the seriousness of the prognosis of Essential Hypertension.

These observations are further supported by a few individual case records

*Case I*—M 76 GB 36 yrs F BP on admission 165/110 Bl Urea 22 mg %. Retinopathy grade I First ERG on 4.5.60 Av b pot 252mV. Clinical condition improved with hypotensive drugs. ERG repeated 9½ months later. The electrical potential improved to 45mV. During a follow up of upto May 1962, the patient was under control and asymptomatic. The initial nearly normal response and an increase of b-potential later supported by clinical observations is indicative of good prognosis and the benign nature of hypertension.

*Case II*—M 64 G 40 yrs M, Admitted with BP 220/140 and Bl Urea 24 mg %. Retinopathy grade I First ERG on 23.3.60 Av b pot 282mV. As the patient was not improving with treatment ERG repeated 7 weeks after the first one and the b pot recorded was 132mV. Patient ultimately died 10 days later. The b pot although normal in the initial stage, rapidly becoming subnormal and the patient dying soon after is suggestive of poor prognosis, even though biochemistry and the grade of retinopathy were not indicative of the seriousness of the disease.

*Case III*—M 56 BL 47 yrs M Admitted with BP 260/150 Bl Urea 15 mg % and Retinopathy grade III ERG recorded on 15.3.60 Av b-pot 112mV. Patient died 15 days later. A markedly subnormal ERG in this case further supports the seriousness of the condition indicated by higher blood urea and retinopathy.

*Case IV*—B-10 HL 25 yrs M Admitted with BP 184/122, Bl Urea 10 mg %, but Retinopathy clinically looking grade IV First ERG on 15.3.57 Av b-pot 275mV. Patient clinically improved with treatment and the Av b pot recorded 9 months later b-pot improved to 425mV. Follow up indicated that the patient was well under control for upto 1 yrs thereafter. Although retinopathy indicated the seriousness of the disease but a normal Bl Urea and a normal initial ERG rising still further later on supported by clinical condition

is suggestive that the LRG could be a dependable guide in the prognosis of hypertension and the retinopathy in this case may be due to other factors

**Last Case I**—B & S 52 I II 30 yrs F, Was first admitted with B P 210/110 B I Urea 22 mg % and retinopathy grade II First LRG recorded on 17-3-57 with A v b pot 165mV Patient responded to treatment and left hospital asymptomatic Patient was readmitted for recurrence of symptoms 1 year later with B P 258/110 and B I Urea now risen to 80 mg % and retinopathy now grade III Second LRG recorded on 19-3-58 A v b pot 125mV Patient left the hospital against advice after some symptomatic improvement but returned again 3 months later with B P 255/170 B I Urea mg % and retinopathy now grade IV A v b pot recorded on 21-6-58 was 069mV and the patient died a month later on 21-7-58 In this particular case, if we go back to the findings at first admission 1 year and 4 months before death, neither retinopathy grade II nor B I Urea 22 mg % was indicative of the seriousness of disease Distinctly subnormal LRG at that stage was the only indication suggestive of oncoming seriousness of the disease which was supported by subsequent findings and the ultimate death

On the basis of these studies, I make the following suggestion —

- 1 That a subnormal response in a case of clinical hypertension may be suggestive of oncoming malignancy at a later date and therefore should be an unpleasant finding
- 2 Falling b potential during repeated ERG, is still more indicative of the possibility that a clinically benign hypertension may be the beginning of malignancy
- 3 LRG may be a fairly dependable means of assessing the prognosis of a particular case of hypertension even at a stage when neither retinopathy nor bio chemistry of blood are a helpful guide
- 4 LRG should be a routine procedure of investigation in all cases of essential hypertension

## USE OF AN AVERAGING COMPUTER IN ANALYSIS OF THE HUMAN ERG

JERRY H JACOBSON, M D

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GEORGE STEPHENS, M D

*New York—US 4*

As investigators have pursued the analysis of the electroretinogram further and further in detail attempting to exact as much information as possible from their records measurement and study of small sub components of the ERG as well as detection of minute responses, have become a problem of increasing interest

Several approaches have been made to increase the ability of our recording and amplifying system to provide the information we are all seeking

If we assume that satisfactory amplifier design is utilized of necessity the limiting factor in such minutious seeking is the recording system

There are several types of recording system in use each with its own advantages and drawbacks We wish to present our experience with one which we consider has several great advantages

The ink writing electroencephalograph machine has one great advantage over all others It is simple foolproof and sturdy For recording of the gross features of the ERG response I believe it is highly satisfactory and still forms the basis of much of our clinical work There are however, several disadvantages to its use Because it is an electromechanical device in which the mass of the pen must be moved there is a definite inertia to the system which induces a loss of the fast portions of the response

This loss of fast response is overcome if a cathode ray oscilloscope is used as the recording device This device by virtue of its minimal distortion since the only inertia is due to the infinitesimal mass of the electrons which are the indicator, is much more responsive to fast changes It however required some sort of photographic technique for permanent registration of results and thus may result in delay in interpretation of results

In addition since each record may contain a few minute elements of the response or an extremely minute response, it is only by comparison of a large series of such photographs that one can be certain of the presence with regularity of some small sub-component of the response

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**Last Case V—** B & S 52 L II 30 yrs F, Was first admitted with B P 240/140 Bl Urea 22 mg % and retinopathy grade II First LRG recorded on 17-3-57 with Av b pot 165mV Patient responded to treatment and left hospital asymptomatic Patient was readmitted for recurrence of symptoms 1 year later with B P 258/140 and Bl Urea now risen to 80 mg % and retinopathy now grade III Second ERG recorded on 19-3-58 Av b pot 125mV Patient left the hospital against advice after some symptomatic improvement but returned again 3 months later with B P 255/170 Bl Urea mg % and retinopathy now grade IV Av b pot recorded on 21-6-58 was 069mV and the patient died a month later on 21-7-58 In this particular case, if we go back to the findings at first admission 1 year and 4 months before death, neither retinopathy grade II nor Bl Urea 22 mg % was indicative of the seriousness of disease Distinctly subnormal LRG at that stage was the only indication suggestive of oncoming seriousness of the disease which was supported by subsequent findings and the ultimate death

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to go off at the time of the 20th memory cell. This allows the observation of the base line of activity *prior* to the stimulus. As the first response is obtained each memory is charged with an amount of potential proportional to the amplitude of the response at its particular moment in time. Each following response then adds to the charge in the particular memory at the identical time relative to the stimulus light. It is possible to obtain in this manner several hundreds or thousands of responses and to store in the series of memories, the SUM of the electrical potential of all of them, at each point in time.

The instrument is operated on line, that is directly connected to the patient by way of an amplifying system and slide 2, the summed response is visible, as the sum is accumulated, on the face of a cathode ray tube in the panel. This on line feature eliminates much of the difficulty found in the use of the tape recording system described above.

Since this device is synchronized with the stimulus flash the electrical events which occur at the same time after each will be superimposed and hence reinforced. Random eyeball motion, power line and other artifactual electrical noise will not occur at the same time after each response and such contaminants of our records are statistically cancelled. When the desired number of responses have been recorded one may photograph the face of the CRO tube, or use an X-Y recorder or other device to obtain a permanent record.

This device has therefore the advantages of allowing us to obtain the sum of a large number of responses and to cancel out erroneous factors and we believe hence to achieve our aims of increased fidelity of recording of fast components as well as minute ones.

I should like to show you a few examples of what the instrument will do (Slide 3). This is a patient with a retinal degeneration in whom using a standard inkwriting technique—and incidentally, although not shown on the slide, also using a CRO, only a minimal response is demonstrable. By summing 100 responses, however, it is possible not only to be sure that the response observed is not an artifact but to observe certain of its characteristic conformations.

Slide 4. This slide shows the ability of the device to record the characteristics of fast flickering responses—here up to 80 per second. It is to be noted that when the inkwriter records only a smooth sine wave form we are able to discern a non sinusoidal pattern.

Slide 5. Utilizing this technique following the lead of Heck and Rendahl who first reported using the CRO the presence of small components of the response we were able to confirm their findings as shown on slide 5.

The increased fidelity of this technique removes the possibility of these being artifacts. Slide 6 shows a comparison of the time relationships obtained by Heck and Rendahl below and by Jacobson and Suzuki above. Recently we confirmed some of their findings in colour

Some of this difficulty may be eliminated by the use of multiple exposure tracings, such as *slide 1* but when a large series of responses are thus recorded, the result may be an incoherent blur.

Harold Henkes has advocated another technique for recording of multiple responses using a frequency tuned amplifier but, while this may present evidence of some activity at a particular frequency—and, if this frequency is that of a stimulus light—it may be adduced that there is a response in an eye which had not produced a response of measurable proportion by other techniques. The shape of the response is however, grossly distorted by this instrument. Recently, we have had access to an averaging computer.

This development of electronics has allowed us to pursue the aims of increased fidelity of recording the LRG with a series of new instruments. The aims of these techniques are the same two outlined above:

- (1) Increased capacity to measure fast components of the response and
- (2) Increased capacity to record minimal potentials and minute sub components.

Our first approach was the utilization of the tape recorder. There exist instruments of this type in which the signal (as we may call the LRG) is allowed to modulate the frequency of a carrier wave, similar to the technique used in FM broadcasting. By this technique very accurate records of the potential may be obtained. If a series of responses are thus recorded on a length of tape, a device can be utilized which will allow us to make a "closed loop", or endless belt of this tape and play it over and over again through a playback head. It is possible then to sample the amplitude of each response at a given PERIOD after the stimulus light flash and to integrate or sum up the amplitude of the response at, let us say 10 milliseconds after the stimulus in each of 100 responses. This sum can be permanently recorded and the machine now reset to provide this type of sum at 20 milliseconds after the stimulus response. The sums can be drawn sequentially and the total curve of the 100 responses will be obtained.

We were deeply involved in this technique, which I regret to say, in our hands at least, was beset with technical problems—when a new instrument became available. This device, which is called a "computer of average transients" is basically a series of electronic memories, really, capacitors capable of storing an electrical potential and of releasing this charge at demand into a recording system. Each of the 100 such memories in this device is made to correspond to a given instant of time. Thus if we choose to study the electrical activity of the eye beginning ten milliseconds before stimulation and to continue to observe the response for a total of one tenth of a second, each of the memories is set to be equivalent to 1/1000 of a second.

In use, the memories at the beginning of an experiment are all emptied of charge, and the timing circuit of the device is set so as to provide stimuli at the desired frequency through a triggering circuit which controls the stroboscopic light source. This flash is usually set





male of 30 years with active pulmonary tuberculosis and bilateral Eales's disease who died six years later after pneumonectomy, the uvea was entirely normal and the filtration angles widely patent. Using PAS stain Wagner and Contrads (1959) found changes in the ground substance of the venous walls which they attributed to lytic processes resulting from an antigen antibody reaction.

Very few of these changes can be claimed to be specific for Eales's disease. Yet the whole combine to present a characteristic picture of a chronic low grade grumbling inflammatory reaction with degenerative and proliferative changes.

### Aetiology

#### TUBERCULOSIS

The concept that Eales's disease is due to a direct infection of the retinal vessels by tubercle bacilli is not very convincing. The history of the evolution of this theory has been traced in detail by Donders (1958) and it is based on four points. First upon the undoubted association of Eales's disease with cases of active tuberculosis; secondly upon the presence of giant cells and granulation tissue around the vessels; thirdly upon the demonstration of tubercle bacilli in the vicinity of the vessels on four occasions (Gilbert 1914, 1935, Otori 1915, Frank 1925, Stock 1937) and fourthly upon the experimental production of retinal periphlebitis by the injection of tubercle bacilli (Finnoff, 1924 a b, Uyama, 1936, Meyer 1940). Against this it should be noted that many cases of Eales's disease have been reported where there has been no evidence whatsoever of tuberculous infection; a granulomatous reaction, even if tuberculous in appearance, can be simulated by other disease entities. The finding of tubercle bacilli on so few occasions suggests that these positive cases may belong to a different category, probably to miliary tuberculosis (Goldstein and Wexler 1930) while the experimental lesions bear little resemblance to Eales's disease. To me it seems inconceivable that infection with tubercle bacilli could give rise to such a restrained and diffuse inflammatory reaction as seen in periphlebitis.

There is however good reason to suppose that tuberculosis may play some role in a proportion of cases. For the not infrequent association of Eales's disease and active tuberculosis in young individuals appears too striking to be dismissed as a chance occurrence. In India for instance Eales's disease has a higher incidence than in Western countries and this has been attributed to a higher incidence of tuberculosis (Gupta 1938).

On theoretical grounds it would seem entirely possible that the retinal vessels may become selectively sensitized to tuberculo-protein and that an allergic vasculitis results when the vessel are again subjected to this antigen. Experimentally, animals pre-treated with intra-ocular tuberculin developed retinal vasculitis when tubercle bacilli were later introduced into the circulation (Uyama 1936, Meyer 1940).

# THE EFFECTS OF SEROTONIN, RESERPINE AND JB-516 ON THE ERG

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Adrenalin and acetylcholine have been studied extensively in the stimulus conduction mechanism of the central nervous system. Catecholamines and serotonin, however, have been investigated intensively in the same field only in recent years.

Ewart, Page, Brodie and others doing research work of the brain have found out many details about the natural occurrence, tissue distribution, biosynthesis and many other functions of serotonin.

However, the significance of serotonin in ophthalmology is almost unknown as yet. Its existence in the retina seems to be proved by a histochemical demonstration of the changes in the monoaminoxidase activity that occur in the rabbit retina after the intravenous administration of serotonin according to experiments carried out by Hojima and other collaborators of our department of ophthalmology.

Here we report the results of our research work concerning the function of serotonin in the retina from the electroretinographical point of view.

## MATERIAL METHOD

Albino rabbits on which no general anesthesia was performed and in whose eyes mydriasis was produced by a one per cent atropine solution were dark adapted for half an hour before their ERGs were recorded.

The recordings of ERGs extended over a period of about 48 hours and the different effects caused by the various substances injected intravenously were as follows. For the light stimulation, Buffington's photic stimulator and a contact lens electrode were used. The amplitude of the a- and b-wave were measured, compared and studied.

## RESULTS

1. Effect of serotonin. The amplitude of the b-wave decreased evidently half an hour after the administration of a relatively large dosage of serotonin (30 mg/kg) and this effect continued for about 48 hours. A series of subsequent studies with dosages of 20, 10 and 5 mg/kg respectively indicated that a dosage of 20 mg or less caused no changes. From these facts I suggest that there is a blood-retinal barrier for this substance.

blind individuals. The complete paper dealing with this subject will be published shortly in the AVIA Archives of Ophthalmology, but this is a composite slide to show some of the alterations of responses obtained in several forms of colour deficiency.

Slide 7 shows how effectively this device will screen out sixty cycle artifact from the power lines.

To sum up, therefore, we believe that this averaging computer, while certainly not the *ultimate* instrument for recording of the LRG, is, in our opinion, the best yet *available* for observation of fine, fast components of the response. Its disadvantages are its cost and the fact that it is a statistical averaging device, which may compromise the characteristics of each of a series of responses, i.e., make it possible to determine how the first of a series may vary from the *sequential* ones. In order to overcome this objection we routinely record simultaneously with the CRO and the inkwriter, in those instances where this is important.

# THE EFFECTS OF SEROTONIN RESERPINE AND JB 516 ON THE ERG

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Adrenalin and acetylcholine have been studied extensively in the stimulus conduction mechanism of the central nervous system. Catecholamines and serotonin, however, have been investigated intensively in the same field only in recent years.

Iwarog, Page, Brodie and others doing research work of the brain have found out many details about the natural occurrence, tissue distribution, biosynthesis and many other functions of serotonin.

However, the significance of serotonin in ophthalmology is almost unknown as yet. Its existence in the retina seems to be proved by a histochemical demonstration of the changes in the monoaminoxidase activity that occur in the rabbit retina, after the intravenous administration of serotonin according to experiments carried out by Hojima and other collaborators of our department of ophthalmology.

Here we report the results of our research work concerning the function of serotonin in the retina from the electroretinographical point of view.

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The recordings of ERGs extended over a period of about 48 hours and the different effects caused by the various substances injected intravenously were as follows. For the light stimulation, Buffington's photic stimulator and a contact lens electrode were used. The amplitude of the a- and b-wave were measured, compared and studied.

## RESULTS

1. Effect of serotonin. The amplitude of the b-wave decreased evidently half an hour after the administration of a relatively large dosage of serotonin (30 mg/kg) and this effect continued for about 48 hours. A series of subsequent studies with dosages of 20, 10 and 5 mg per kg respectively indicated that a dosage of 20 mg or less caused no changes. From these facts I suggest that there is a blood-retinal barrier for this substance.

(2) Effect of reserpine The evident decrease of the b wave could be observed within one hour after the administration of 2 mg per kg of reserpine, but its effect continued for about 24 hours

It is well known that reserpine has the effects of a general sedation and mild depression on the blood pressure Brodie and others found that following an intravenous administration of reserpine, the brain level of this substance reached its peak in half an hour and decreased rapidly thereafter, while that of serotonin fell to a low in about one hour where it continued for approximately 36 hours, after which a gradual recovery began This fact indicates that mild and long acting pharmacological effects of reserpine are caused by the serotonin it releases Assuming that the mechanisms in the brain are the same as those in the retina, it can be inferred from the above facts that the decrease of the b wave in the ERG is a secondary effect of serotonin in its free form, that is, released by reserpine

(3) Effect of JB-516 Then, we studied the effect of JB 516, a strong inhibitor of monoaminoxidase, which causes an abnormal accumulation of monoamines such as catecholamines, serotonin and others in the tissue Slight elevation of both, the a- and b wave could be observed after the administration of 3 mg per kg of JB 516 This effect of JB 516 on the ERG continued for about 20 hours

Krill reported an experiment in which LSD 25 was applied as a hallucinogenic substance rather than as an inhibitor of MAO He observed an enlarged b wave in the human electroretinogram and a disturbance of dark adaptation after LSD 25 was administered and he considered this increase of the b-wave as due to a functional disturbance of the retina caused by LSD 25 We considered that these electroretinographic changes, were the result of the retinal hyper excitation caused by amines, such as serotonin, which accumulated above the normal level under the effect of JB-516

(4) Effect of JB 516 and reserpine combined The changes of ERG were followed up after reserpine was administered to a rabbit pre medicated with JB 516 When 2 mg per kg of reserpine were administered 24 hours after the administration of 3 mg per kg of JB 516, the decrease of the b wave was much more noticeable than after an application of reserpine alone This fact may imply that much of the serotonin was soon after released due to the influence of reserpine, as the noticeably decreased b wave reflected

(5) Effect of chlorpromazine For comparison with the effects caused by the substances used so far, we now applied chlorpromazine The administration of 3 mg per kg of chlorpromazine caused only a short, transient decrease of the b wave, not prolonged as serotonin produced it, which seems to be the effect of a different mechanism

(6) Effect of esidrex Esidrex, another blood pressure depressant, turned out to show hardly any effect on the electroretinogram

(7) **Histochemical findings** It was observed that the serotonin MAO existed in an normal rabbit retina and the activity of the serotonin MAO was changeable caused by the administration of serotonin (30 mg/kg) reserpine (3 mg/kg) and JB-516 (3 mg/kg)

### SEROTONINE

ERB et Serotonine par Mme Samson — DOLLFUS (Discussion de la communication de M Juiduro Sugita)

Le hasard a fait que j'ai enregistré, à titre de témoin une malade qui était atteinte d'une caranoidase avec départ de intestin grêle, sécrétant la serotonine

J'ai toujours hésité à placer ce sujet dans mes témoins, malgré tous des ophtalmologistes qui n'avaient à me proposer aucun signe clinique au fond de l'œil. En effet cet ERB ne me paraissait pas assez ample. Je l'ai vu enregistré peu après l'épreuve au porto qui favorisait la sécrétion de serotonine

Rétrospectivement, je me demande si cet ERB, dont l'amplitude globale était diminuée n'était pas due à la sécrétion de serotonine

### SUMMARY

After studying the respective effects of intravenously administered serotonin reserpine and JB-516 on the ERG, we consider that the release of serotonin in the retina decreases the b-wave while abnormal deposits of serotonin increase it. The histochemical studies proved that serotonin existed in an normal rabbit retina. Summing up we can say that serotonin plays an important role in the stimulus conduction mechanism of the retina.

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## METHODE

Nous nous sommes fait un devoir d'étudier comment varient la grandeur et la forme de l'ERG avec les différentes largeurs de la pupille. L'ERG était enregistré à l'aide d'un électro-encéphalographe WFBG à 11 conduites. Après avoir provoqué chez le malade une mydriase artificielle on adaptait le malade pendant 5 minutes à la lumière de 25 lx. Pour l'examen on avait choisi des individus âgés de 18 à 30 ans. Les stimulus lumineux de 5 000 lx étaient produits par un éclair électronique d'une durée d'éclair lumineux de 0.002 secondes.

## PROCÉDE DE TRAVAIL

### 1 Dans le premier groupe

Devant l'œil à examiner on plaçait à une distance de 15 mm du sommet de la cornée une plaquette avec une ouverture circulaire dont la grandeur était changée de 0.5 mm à 3.0 mm par 0.5 mm. Dans ce groupe nous avons enregistré au total dans 17 séries 236 ERG évaluables.

### 2 Dans le deuxième groupe

Sur la lentille de contact nous avons placé une pellicule ayant une ouverture circulaire dont nous avons changé le diamètre en changeant les pellicules de 1.0 — 1.0 mm toujours par 1 mm. Nous avons enregistré dans 20 séries 320 ERG évaluables et pour comparer les résultats nous avons choisi les malades du premier groupe.

### 3 Dans le troisième groupe

Comme stimulateur nous nous sommes servis au lieu de l'éclair électronique des rayons lumineux à une divergence de 5° et une grandeur lumineuse de 200 lx. Nous en avons illuminé la région centrale pendant un temps de stimulation de 0.01 sec. L'ouverture circulaire dans la plaquette était placée devant l'œil sous les mêmes conditions comme au premier groupe. Nous avons enregistré en 18 séries 352 ERG évaluables.

### 4 Infirmité

Nous nous sommes servis de lentilles de contact qui à l'exception de l'ouverture circulaire au centre ayant un diamètre de 2 mm étaient fabriquées d'un matériel tout à fait opaque. Ce groupe devait vérifier dans quelle mesure le facteur de la lumière dispersée pénétrant du côté et le facteur de la lumière passant par le sclère pourraient de former l'ERG. Nous avons enregistré en 15 séries 130 ERG évaluables.

## RESULTATS

Dans les valeurs moyennes du premier groupe examiné on pouvait observer que l'onde a et b accroît avec la grandeur de la surface de l'ouverture de la plaquette préposée. En plus on pouvait remarquer une diminution de la somme du temps de latence du temps de durée de la composante positive de l'onde b. Il nous intéressait surtout

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Le problème de stimulus lumineux joue un rôle important dans des grands efforts que l'on fait pour standardiser les méthodes électroretinographiques. L'étendue de l'illumination de la rétine sort de mesure de l'irritation des photorécepteurs réagissant à la lumière. Cette illumination de la rétine [1] dépend de toute une série de facteurs. Ce sont la clarté de la source lumineuse [B], la pénétrabilité du milieu [d], la surface de la pupille [Fp], la distance objective focale de la source lumineuse [f]. D'après Schober [1] la dépendance suivante est valide:

$$I = \frac{d \cdot B \cdot F_p}{f^2}$$

Aujourd'hui nous allons nous occuper du facteur de la surface de la pupille qui est important pour l'étendue de l'illumination de la rétine. L'étendue de la surface de la pupille a de plus aussi une grande influence sur le cours de l'adaptation. La largeur de la rétine est donnée par les faits régulateurs nerveux les influences psychiques, l'état malingre, l'âge etc. Heringer [2] a étudié la question de l'influence de l'âge sur la largeur de la pupille. Mise à part la période de l'enfance et de la senilité, la largeur se trouve d'après Schober dans une dépendance linéaire au logarithme de l'illumination. La largeur de la pupille varie entre 1,5 et 8 mm. C'est à dire que la surface de la pupille varie entre 1,7 et 50 mm<sup>2</sup>. La surface de la pupille a donc une grande influence sur l'étendue de l'illumination de la rétine. On sait que l'étendue de l'illumination de la rétine détermine la grandeur et la forme de l'ERG. De cette question s'occupent déjà tout un nombre d'auteurs comme Asher [4], Boynton [5], Gied, Grunt [6], Irey, Bartley [7], Grunt [8], Grunt Rubinstein, Ihorman [9], Kupe [10], Kuffler [11], Riggs Berry, Wyner [12], Wirth, Zetterstrom [13] et autres. Les résultats donnés par les divers auteurs ne sont pas identiques. Nous voulons vérifier les résultats de nos études précédentes non publiées de l'année 1958 que l'onde b augmente linéairement avec l'augmentation logarithmique de la surface de la pupille artificielle ce qui correspond à la loi généralement valide de Weber Fechner qui dit que la perception augmente linéairement avec le logarithme de l'excitation.

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The fibrous strands arising from the retina, and which ultimately lead to its detachment, are particularly characteristic, appearing tubular in section with a fibrous core and a cellular covering (fig 9), they extend in a serpentine fashion from the inner substance of the

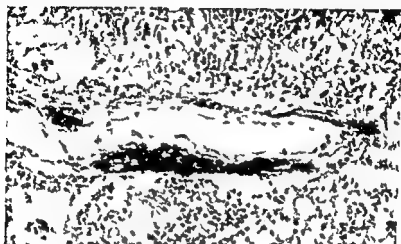


FIG 8 Eales's disease Flat section of retina showing hyaline thickening of a small vein and perivascular pigmentation Haematoxylin and eosin  $\times 280$



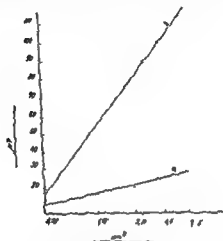
FIG 9 Eales's disease Fibrous strand in the vitreous arising from the retinal surface Haematoxylin and eosin  $\times 112$

stratum opticum and course along the face of the vitreous in areas where it is detached. In fact the vitreous detachment appears to be intimately concerned in their formation.

From my own pathological examinations it would seem that uveitis is not an essential accompaniment. In one typical case, in a

et sur l'axe y le potentiel de l'onde a et de l'onde b. Le graph indique que même ici il n'y a pas de dépendance logarithmique.

3 Dans le troisième groupe où nous avons employé un stimulus de 200 Lx avec une exposition prolongée de 0,002 à 0,01 secondes nous avons porté la moyenne des résultats sur le graph 3 qui montre une augmentation linéaire de l'onde a et de l'onde b avec une augmentation logarithmique de la surface de l'ouverture artificielle.

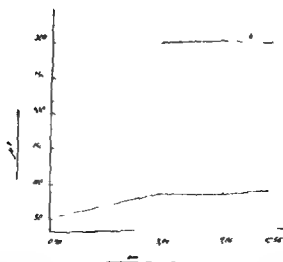
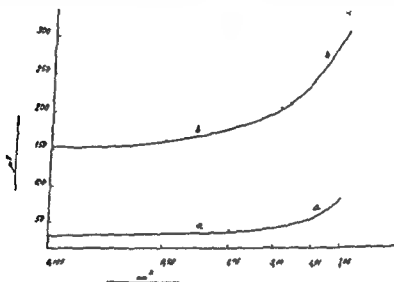


4 Dans le quatrième groupe examiné à l'aide d'une lentille de contact en matériel opaque et une ouverture au milieu d'un diamètre de 2 mm nous avons pu comparer les résultats obtenus à l'aide d'une ouverture de la même grandeur. Les valeurs moyennes des potentiels de l'onde b étaient plus petites que celles obtenues avec les ouvertures du même diamètre dans les autres groupes et un signe frappant de ce groupe était qu'en se servant de l'éclair électronique les séries des ERG étaient par la forme du développement de l'ERG égales en comparaison avec les examens en série des groupes précédents.

#### DISCUSSION

Pour le moment il est difficile de dire quelle est la largeur la plus avantageuse de la lentille artificielle. Par rapport à l'intensité lumineuse de l'éclair électronique nous pensons que l'ouverture la plus avantageuse était l'ouverture circulaire jusqu'à 2 mm de diamètre. L'élimination de l'influence de la lumière dispersée est un autre élément intéressant provenant d'un parcours différent des courbes obtenues par la préposition de la plaquette en utilisant un éclair électronique et des rayons presque parallèles du stimulus lumineux. La meilleure loi présumée et exprimée de l'augmentation de l'onde a et de l'onde b d'après la loi de Weber-Fechner semble dépendre dans les rayons presque parallèles du stimulus lumineux surtout de l'élimination de la lumière dispersée.

quelques unes de ces courbes s'approchent du parcours logarithmique et c'est pourquoi nous avons designé les résultats moyens dans certains exemples dans le tableau 1 et dans le graph 1 ou sur l'axe  $x$  est portée la surface de l'ouverture dans une échelle logarithmique et sur l'axe  $y$  le potentiel de l'onde  $a$  et de l'onde  $b$ . Dans la largeur physiologique de la pupille on peut observer avec la surface augmentante de l'ouverture une augmentation de l'onde  $a$  et de l'onde  $b$ . En comparant le parcours entier il ne s'agit pas d'une dépendence logarithmique continue.



2 La moyenne des résultats obtenus au deuxième groupe avec les pellicules est donnée dans quelques exemples au tableau 2 et au graph 2, ou sur l'axe  $x$  est portée la surface dans l'échelle logarithmique





Diamètre de l'ouverture circulaire dans la pellicule

Mat ade	Oeil	40 mm			30 mm			20 mm			10 mm		
		Diamètre du potentiel = micro V		mojeune en cm lignes de sec	a	b	t	a	b	t	a	b	t
		a	b	t									
1	OD	68.2	256.0	—	47.4	232.0	—	—	—	—	39.8	205.0	—
	OS	91.0	278.0	—	57.5	256.4	—	—	—	—	45.2	230.8	—
	Moyenne OD + OS	74.6	267.0	—	53.4	244.2	—	—	—	—	42.5	217.9	—
2	OD	70.5	266.0	7.6	109.5	321.0	7.0	100.0	310.0	7.1	98.5	176.5	11.3
	OS	80.0	295.0	6.9	91.5	304.0	7.0	93.5	386.0	7.0	99.8	163.5	8.1
	Moyenne OD + OS	75.2	280.5	7.2	100.5	369.0	7.0	96.7	363.0	7.0	99.1	165.0	9.8
4	OD	74.5	246.0	4.8	115.0	341.0	5.2	123.8	238.0	7.3	18.7	231.0	7.1
	OS	163.0	455.0	4.9	146.0	491.0	5.3	141.0	482.0	7.1	96.0	407.0	6.9
	Moyenne OD + OS	118.7	350.5	4.8	130.5	419.0	5.2	132.4	390.0	7.2	72.3	319.2	7.0
5	OD	83.3	230.0	6.4	87.2	240.0	7.3	66.0	244.0	8.0	51.8	201.0	7.0
	OS	101.0	368.0	5.3	83.2	317.0	7.8	81.6	306.0	7.0	73.0	232.0	7.1
	Moyenne OD + OS	92.1	299.0	5.9	86.2	283.5	7.8	83.8	267.8	7.5	68.2	262.6	7.7
7	OD	66.0	270.0	6.9	36.8	137.0	6.4	33.0	201.0	6.1	21.1	103.0	6.3
	OS	111.0	290.0	6.2	33.2	266.0	6.6	36.6	137.0	6.8	23.4	137.0	6.9
	Moyenne OD + OS	85.2	278.5	6.9	47.3	223.4	6.5	34.8	199.0	6.7	22.4	164.6	6.6
Moyenne totale		88.4	295.2	—	87.2	303.3	—	85.2	301.8	—	80.8	216.9	—
Nombre des mesurages		6.3	65	33	75	7.3	63	54	34	34	7.3	77	65

## DISCUSSION

### ELECTRO DIAGNOSTIC TEST BASED ON THE STANDING POTENTIAL OF THE EYE

ARDEN, G B (U A)

Electrodes placed on the skin over the eyes record potentials associated with eye movements which can be used to estimate the magnitude of the intra ocular potential generators. These vary in size as retinal illumination is altered with a time course demonstrating that the potential is related to the metabolism of the outer retina. The clinical test (the EOG) based on these findings can be used in the diagnosis of many types of retinal lesion and is especially sensitive in the detection of degenerations and abnormalities in blood supply

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### EXPERIMENTAL STUDIES ON THE EYE MOVEMENT BY MEANS OF SIMULTANEOUS RECORDING PHOTO ELECTRONYSTAGMOGRAM

HATAKEYAMA AKINI (Japan)

A new arrangement of the photoelectronystagmogram (PNG) has been designed as follows. The image of the subject eye is focused by a telelens on the narrow slit set up in front of a photomultiplier tube. The image of the iris and the sclera is allowed to situate on the narrow slit after simple adjustment through a window which is opened on the upper corner of the optical box. In order to carry out our experiments two optical systems of the same structure were prepared.

Firstly PNG of horizontal components of right and left eye has been recorded simultaneously. Secondly we have recorded the diagonal component at angles of 45 and 135 degrees on one eye and thirdly we recorded eye movement with one system and the face movement with the other.

From these experimental results the relationships between optokinetic nystagmus, fixation reflex and fusional movement of each eye have been discussed.

La constance relative des courbes de l'FRG en employant des lentilles opaques avec une pupille artificielle de 2mm semble être une recommandation pour l'emploi de cette lentille pour l'œil cycloplegique pour la standardisation de la méthode

### CONCLUSION

Les quatre groupes des résultats présentes semblent indiquer que les recherches sur l'influence de la pupille sur l'FRG devraient étudier

1 L'intensité la plus favorable de stimulus lumineux du point de vue de la loi Weber-Fechner

2 Assurer à la pupille artificielle dans la lentille de contact la quantité standard de lumière entrant l'œil

3 Éliminer l'effet de la lumière dispersée et de la lumière passant aussi par le sclère

### La littérature

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- 2 Schober Das Sehen I 60
- 3 Schober Das Sehen I 61
- 4 Asher H 1931 *J Physiol Lond* 12 40
- 5 Boynton R Riggs L 1931 *J exp Psychol* 42 217
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- 7 Irey C Bartley S 1933 *Imer J Physiol* 111 335
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- 11 Kuffler S W 1933 *J Neurophysiol* 16 137
- 12 Riggs L Berry R Wyner M 1949 *J Ophth Soc Amer* 39 427
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however, an electro oculogram (EOG) could not be recorded before the subject was able to cooperate voluntarily, producing eye movements necessary for the measurement of the standing potential

The present paper describes, among other things a technique which has been developed for the recording of the FOG in children in narcosis. The procedure described is applicable and has been applied already shortly after birth

The results of such a combined electro diagnostic procedure in children suspected of developing tapeto retinal degeneration of various origin are discussed

## PROCEDURE

In the standard recording of the ERG, both single flash and flickering light stimuli have been applied. The single flash technique (using a blue filter (Gevaert B 488)) is particularly meant for the recording of scotopic activity. The flicker ERG using the technique of selective amplification of the flickering response (Henkes, van der Tweel and Denier van der Gon (3)) is recorded in order to be able to construct an I/CFF curve (intensity versus flicker fusion frequency) for the photopic mechanism using arbitrarily the following frequencies 20 30 40 60 and eventually 70 flashes per second. Stimulus source electronic stroboscope (van Gogh) with frequency independent intensity steps of relative intensity 1 2 4 8. Reduction in intensity is done with the help of neutral density filters of a factor 8 and 64. Recording apparatus 6 channel van Gogh EEG machine with 1-channel frequency analyser. The time constant used for the recording of the single flash ERG is 1 second for the recording of the flicker ERG 0.03 sec. — Normal range of maximum scotopic b wave (measured from the trough of the a wave — if present —) varies between 250 and 530 microvolts. Values lower than 210 microvolt, are considered probably subnormal and lower than 180 microvolts to be definitely subnormal.

Normal limits of I/CFF curve is given in the figures. Aberration from the normal course is judged referring to the standard curve.

The standard recording of the FOG — giving information concerning the standing potential of the eye — asks for excursions of the eye over a given angle — in our setup 30 degrees — in the horizontal plane which produces a potential difference between electrodes mounted on the temporal and the nasal margin of the orbit (figure 1 a). The potential produced varies among other things with the adaptive state of the retina (figure 1 b). The FOG potential partly derives from the corner. This part is of the opposite sign and reduces the final potential recorded.

Our standard technique of FOG recording is essentially the same as used by Arden recording of the FOG in dark adaptation up to 12 minutes. Light adaptation (adapting level 20 000 Trolands) and continuation of recordings every minute to approx. 30 minutes. Reduction or loss of FOG refers primarily to the change in voltage

## THE ROLE OF ELECTRORETINOGRAPHY AND ELECTROOCULOGRAPHY IN THE EARLY DIAGNOSIS OF TAPETO RETINAL DEGENERATION IN CHILDREN

H. I. HENKIS, M.D. and P. C. VTRDUIN, M.D. (1)

(Eye Clinic, Rotterdam Medical School, Rotterdam)

### INTRODUCTION

In the early diagnosis of retinal disorders of degenerative origin the application of combined diagnostic techniques seems to be essential. Apart from the indisputable value of electroretinography as a diagnostic tool of primordial value electro-oculography comes more and more to the fore (see Arden's paper of this meeting).

Nowadays we know that photoreceptors, bipolar cells and the inner retinal cell systems belonging to the two retinal mechanisms, all contribute to the development of the ERG.

On the other hand, the condition of choroid, Bruch's membrane, pigment epithelium and outerlimbs of the photoreceptors is reflected in the standing potential of the eye. The recording of this potential seems thus crucial for the objective judgement of the functionality of these structures.

It is clear that both recordings, of ERG and LOG, are necessary in order to get the maximum information regarding the function of retina and choroid.

According to Arden and co-workers (1, 2), the initial stages of degenerative retinal affections can be diagnosed more readily while using an electro-oculographic examination. The alterations demonstrable in the FOG recording are said to precede those found in the ERG.

Karpe (2) reported already a number of years ago that an extinguished ERG had been found in an ophthalmoscopically normal child of 7 months, of a mother suffering from a dominant tapeto retinal dystrophy. In most cases, however, the affection is said to develop at a later stage.

All in all, electro diagnostic procedures seem to be essential in the examination of those children, who are prone to get a degenerative retinal affection even before fundal changes have appeared. The latter are, as we know, relatively late signs of irreparable alterations of retinal function.

From the above, it is clear that the earlier these diagnostic procedures may be applied, the better. An electroretinographic examination can be performed—as we all know—almost from birth on. Thus far,

(1) The report was produced in cooperation with the Netherlands General Association for Prevention of Blindness.

For the recording of the EOG in the young patient a special technique has been developed (Henkes and Verduin (4)) which copes with the difficulties encountered by the recording in children unable — due to their age — to carry out instructions. The recording is done in narcosis which enables us to carry out the recording even in infants. Besides the narcosis eliminates the troublesome nystagmus if present. Recording is done — as in the standard technique — in dark and light adaptation.

Use is made of low vacuum contact lenses of Worst (5) developed for the localisation of intra ocular foreign bodies. The eyes are mounted with contact lenses provided with an extra long shaft. The shafts of both lenses are fixed in a kind of ruler which is allowed to move in a kind of trial frame over a given distance producing an excursion of the eyes over a given angle of vision (see figures 2 a and b 3). The eyes are forced to move due to the suction system. Simple movement of the ruler is sufficient to produce the desired EOG (\*).

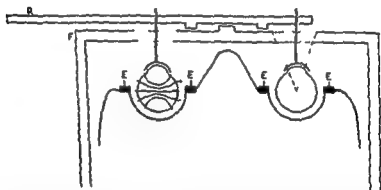


Fig. 1 Schematic drawing of EOG technique applicable in narcosis. The eyes mounted with low vacuum contactlenses provided with a metal shaft are forced to follow movement of ruler (R) while shifted over a given angle.

The FOG produced is essential the same as found under standard conditions

Naturally an exact comparison between the results obtained with the standard technique and this special technique devised for the recording of the FOG in narcosis, is impossible (influence of narcosis on the FOG differences in age difference in angle over which the eyes are moved etc)

( ) The frame and contactlenses etc have been deigned and produced by  
Medical Workshop Herrangel 28 Groningen Netherlands

under the influence of changing conditions of light and dark adaptation. The voltage of the IOG itself is reduced as well. The normal variation in the basic voltage, however, differs even between normal eyes substantially due to the amount of proptosis.

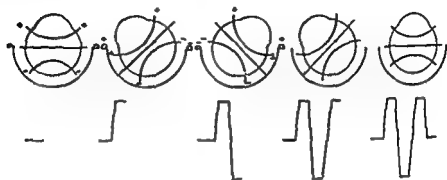
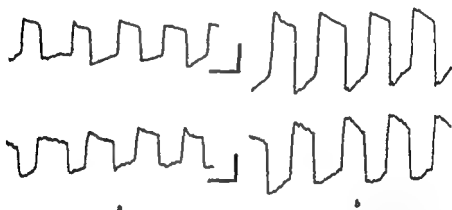


FIG. 1. A Recording of standing potential based upon alterations in the electric field of the eye following eye movements in the plane of the electrodes.



- FIG. 2. The upper tracing of the original graphs records movements of the right eye; the lower of the left eye. The trace begins with a movement of the eyes to the left after which the subjects look rhythmically from one fixation light to another. In between the eye movements the pens return towards the base line owing to the time constant of the amplifiers. The amplitude of the vertical excursions is a measure of the magnitude of the standing potential. (a) after 12 min dark adaptation; (b) 3 min after re-illuminating the retina. Calibration bars: 500 micro Volts/500 msec (after Arden and Kelly, *J. Physiol.* 161: 189-204 (1962)).

According to Arden and co-workers the mean increase in voltage following intensive light adaptation is 252%. An increase of 200% is suspected and an increase less than 185% is considered as definitely abnormal.

viral in which immune mechanisms are especially prominent and in which hypersensitivity is known to develop

### ASSOCIATION WITH NERVOUS MANIFESTATIONS

There seems to be no doubt that retinal perivasculitis can occur in association with nervous manifestations — an incidence of 16 per cent has been quoted (Ballantyne and Michaelson, 1948). The suggestion has been made that this is due to a coincidental periphlebitis of the cerebral vessels (Axenfeld 1921, 1927, 1930) and some of the conditions reported are apoplexy (von Graefe, 1854) convulsions (Ballantyne 1909), transient paralysis (Lowenstein, 1931) polyneuritis (Duvour and Bernard 1933) epilepsy (Haverkorn van Rijsewijk, 1938) paraplegia (Silfverskiöld 1947) and severe headaches (Veurs, 1948), but most notably it has been described in association with multiple sclerosis (Ter Braak and van Herwaarden 1933 Rucker, 1945, 1947, Haar, 1948 1949 1953 Wybar 1952 Gougard and Paris 1954 Hagedoorn 1955 Orban 1955 Paulique and Fuenne 1955 Shubova and Konechakova 1957) in which disease retinal periphlebitis has a reported incidence varying from 10 to 40 per cent (Donders 1958).

It is questionable however, whether many of these cases should be considered in the category of Eales's disease since predominance in the male sex was not always a feature and retinal haemorrhages and retinitis proliferans were frequently absent. Moreover as suggested by Jefferson and Cloake (1952) there is the possibility that the retinal and neurological manifestations may co-exist by chance. It is of interest that recent clinical investigations have obtained contradictory evidence. Thus Silfverskiöld (1947) reported 22 and Jefferson and Cloake (1952) six typical cases of Eales's disease showing no evidence of neurological involvement whereas White (1961) found neurological disorders in seven of 17 typical cases. Conversely Donders (1958) found no evidence of retinal vasculitis in 25 cases of multiple sclerosis whereas Scott (1961) found sheathing of the retinal veins in seven of 65 cases.

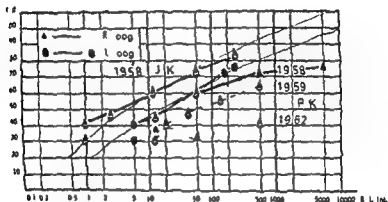
The most recent view is that of White (1961) who maintains that the association is a real one and that the retinal vasculitis is a non-specific inflammatory lesion which probably occurs in the vessels of the parenchyma and meningeal coverings of the brain and spinal cord. According to him the fact that similar lesions may develop in the central retinal vein as originally shown by Ballantyne and Michaelson (1931) and by Verhoeff and Simpson (1940) and more recently by Lyle and Wybar (1961) merely emphasises the anatomical and functional continuity between the retina and the remainder of the central nervous system.

Are we to assume then that Eales's disease is the retinal expression of a vasculitis which may affect the whole central nervous system? This is a crucial question which cannot yet be decided for it appears to be often denied as supported Francis and Neetens (1959) in describing a characteristic instance of sheathing of the retinal veins in a case of

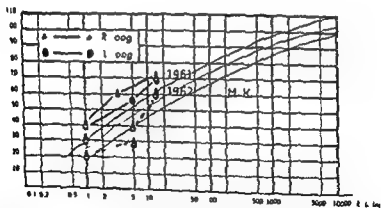


media and fundi normal. In the ERG, the maximum scotopic  $\text{M}$  wave recorded was 250 microvolts in both eyes. The  $\text{I/CFF}$  curve gave a normal course for the photopic retinal mechanism (figure 4 a). The conclusion reached at that moment was that the boy was not prone to get the disease. Up to the present at the age of 8, the boy is completely normal.

4a CFF curve

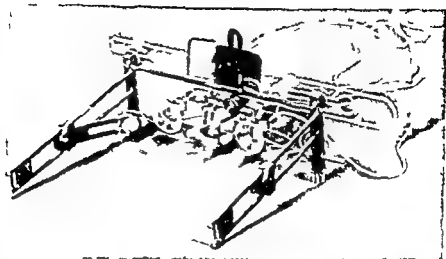


4b CFF curve



4c  $\text{I/CFF}$  curves (photopic branch) of 3 brothers belonging to a family in which a retinomatular degeneration occurs. J.K. shows a normal curve. This child now (1962) 9 years of age developed normally. P.K. and M.K. are affected. The course of the  $\text{I/CFF}$  curves in both children points clearly towards a deterioration of the process. These findings are corroborated by the  $\text{I/OG}$ -data.

(b) His elder brother Peter K. was examined at the age of 6 or the same date as the first examination of Johannes K. There were



B The trial frame ready for mounting



FIG. 3 Child in narcosis mounted with contactlenses and trial frame and prepared for I OG examination

## RESULTS

The value of a combined I RG and I OG examination is demonstrated by the following case reports derived from two families suffering respectively from a cerebro macular degeneration type Spielmeier — Vogt — Bitten — Mayou, and from a tapeto retinal degeneration of intermediate X chromosomal inheritance.

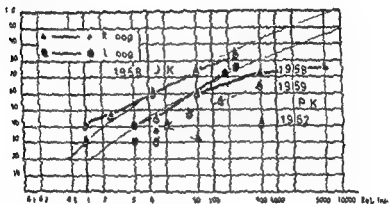
### *Cerebro macular degeneration, juvenile amaurotic idiocy*

We had the opportunity to examine at an early age three siblings of a family in which the above mentioned disease is known to occur

(a) Johannes H. was examined for the first time in 1958 at the age of 5. He had no complaints whatever. Visual acuity 10. Optic

media and fundi normal. In the EFG the maximum scotopic b wave recorded was 250 microvolts in both eyes. The I/CFF curve gave a normal course for the photopic retinal mechanism (figure 4 a). The conclusion reached at that moment was that the boy was not prone to get the disease. Up to the present at the age of 8, the boy is completely normal.

III CFF curve



IV CFF curve

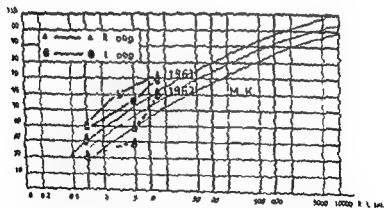
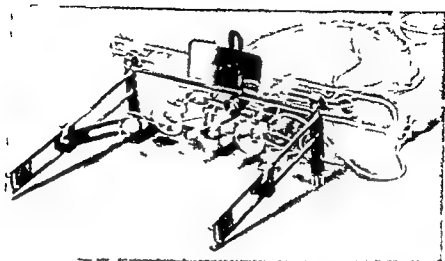


FIG. 4. CFF curves (photopic branch) of 3 boys belonging to a family in which cerebromacular degeneration occurs. J. K. shows a normal curve. This child now (11½) 3 years of age developed normally. P. K. and M. K. are affected. The course of the CFF curves in both children points clearly towards a deterioration of the process. These findings are corroborated by the LOG-data.

(b) His elder brother Peter K., was examined at the age of 6 or the same date as the first examination of Johannes K. There were



II The trial frame ready for mounting



FIG 3 Child in narcosis mounted with contactlenses and trial frame and prepared for FOG examination

## RESULTS

The value of a combined ERG and LOG examination is demonstrated by the following case reports derived from two families suffering respectively from a cerebro macular degeneration type Spielmeier — Vogt — Bitten — Mayou, and from a tapeto retinal degeneration of intermediate  $\lambda$  chromosomal inheritance

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(a) Johannes K. was examined for the first time in 1958 at the age of 5. He had no complaints whatever. Visual acuity 1.0. Optic

(a) Pieter J was examined at the age of 2, in 1961. Optic media and fundi normal. Single flash ERG and flicker ERG normal scotopic and photopic responses. This boy was suspected for having the disease, as a brother was definitely affected. The mother is a carrier of the disease although her fundus oculi does not show the abnormality of a tapetum lucidum like picture described by Falls and Lotterman (5). One year later the fundus had changed in the periphery of the fundus a very slight pigmentary alteration seemed to have appeared. The single flash ERG now revealed a sub-normal scotopic activity (on the right eye a maximum scotopic response of 140 microvolts on the left eye not recordable due to technical difficulties). The photopic I/CFF curve revealed a probable normal photopic activity though due to the technical difficulties encountered the precise interpretation was impossible. The EOG however, supported the ERG finding in as far as the increase in potential following light adaptation was definitely subnormal. It is most probable that this boy will be clearly affected within a relatively short period.

(b) Johannes B. a healthy boy of 2 years of age, had no alterations whatever. His grandfather of mother's side is known to suffer from the disease. His mother and Pieter J's mother are sisters. His mother does not show any abnormalities in the optic media and the fundus oculi. The ERG of the boy was completely normal regarding the single flash — and the flicker ERG responses.

At the renewed examination one year later neither media nor fundi showed abnormalities. The ERG and the EOG however showed definitely alterations which point towards the existence of the disease. The scotopic response is subnormal, the increase in light adaptation in the EOG is lacking (see figure 5). It is clear that this boy at the age of 3 shows already the affection clearly in the electrophysiological results.

(c) A. B. a sister of J. B. was 1½ years of age at the time of examination. The fundi presented no abnormalities. However both scotopic ERG — and EOG-data pointed towards a definite disturbance in retinal activity. The maximum scotopic b-potential recorded was 85 and 75 microvolts for right and left eye respectively. The EOG-curve (figure 5) lacked the normal rise after light adaptation.

It closely resembled in its course the ones known from the beginning stages of tapeto retinal degeneration. In this family more heterozygotic female-carriers are known who suffer from severe deterioration of retinal function. For the first time however we were able to diagnose the affection already in a young girl.

## DISCUSSION

From the above it appears that application of electro diagnostic procedures is essential in order to ensure the diagnosis at the earliest possible moment.

no visual complaints. His parents, however, feared that he might be affected as they observed a change in his behaviour, just like they had observed in two elder children (a brother and sister of this boy), who became affected — Visual acuity 1/10. Optic media no abnormalities. Funduscopy doubtful temporal pallor of the discs. Macular region slight alterations. No pigmentary degeneration visible. The ERG showed markedly reduced scotopic responses, the maximum scotopic b potentials being 55 and 70 microvolts. Photopic activity, judged upon the course of the I/CFF curve, showed only a slightly aberrant course (see figure 4a). Diagnosis was made at this moment on the existence of the cerebro-macular degeneration, though still in its initial stage. One year later, his visual acuity was still normal. Funduscopy however, revealed some more atrophy of the optic discs and a possible increase in the slight macular alterations described one year before. Scotopic activity, judged upon the single flash ERG, was completely extinguished. Photopic activity, expressed in the I/CFF curve, was slightly reduced. Three years later, at the age of 10, visual acuity had been markedly deteriorated. Fingers counting at 1 meter in both eyes. The fundi revealed pronounced alterations: white discs, narrow vessels, abundant pigmentary degeneration both in the central area and in the periphery. The ERG was now completely extinguished, except for a rudimentary photopic response, demonstrating only following selective amplification of the flickering response (see figure 4a). The EOG was of very low voltage too. At the same time any increase in voltage following light adaptation was missing (figure 5).

(c) The younger brother, Marinus K., was first examined in 1961, at the age of 2. Neither in the optic media, nor in the fundus abnormalities were found. The ERG was normal: maximum b potentials of right and left eye respectively were 255 and 220 microvolts. The course of the I/CFF curve was normal (figure 4b). Based upon the results available, the prognosis for this child was considered relatively good. However, one year and a half later, at the age of 3, the parents came to us for a renewed examination, as the child seemed to have changed his behaviour. Though funduscopy did not reveal the slightest alterations, the scotopic ERG pointed towards an important loss of retinal activity. Only a rudimentary scotopic response could be demonstrated. Photopic activity however was still almost normal (see figure 4b). The EOG too, was seriously affected. No significant increase followed the intense light adaptation (see figure 5). It is clear that this boy of only 3 years is already definitely affected. The result of both ERG and EOG examination point towards the same bad prognosis.

#### *Intermediate X chromosomal tapeto-retinal degeneration*

In a family in which the above mentioned disease is known to occur, the below mentioned siblings have been examined in which a combined electro-diagnostic examination seemed to be of importance.

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- (4) Henkes H E and Verduin I G. Dysgenesis or abiotrophy? — Thoughts about Leber's congenital amaurosis *Ophthalmologica* 145, 144-160 (1963)
- (5) Worst J and Oster L. 1961 Low vacuum diagnostic contact lenses *Am J Ophthalm.* 51 410-424
- (6) Falls H F and Cotterman C W. 1949 *Chorioretinal degeneration* *Arch Ophth.* 40 682-693

## PERIODICAL VIBRATIONS ON THE ELECTROMYOGRAM OF THE EXTRAOCULAR MUSCLES

KUBOKI TETSUYA and DOMON EMI (Japan)

Since 1953 electromyography of the extraocular muscles has been one of the studies in ophthalmology. However, basic information about these particular muscles has been lacking. We will report here on some basic features of the electromyograph of these muscles, especially the internal rectus.

Fig. 1 As an electrode a single needle electrode made of a steel wire with a diameter of 0.3 mm was applied. It was insulated with paint made of synthetic resin except for the tip. The needle usually was inserted into the muscle through the skin of the orbital margin. This slide shows the needle having been inserted to examine the internal rectus.

Fig. 2 This figure represents three patterns of the electromyograph of an extraocular muscle. The top recording shows single oscillations of a single motor unit. It is obtained with a needle electrode having a very small naked area at the tip. The middle recording shows an interference pattern which is recorded with a needle having a relatively large naked area at the tip. The bottom recording was obtained by our own original method. This periodical wave is the result of summation of single oscillations of many motor units. The chief components of our method are firstly, relatively large naked area on the needle, secondly, some distance between the muscle and the needle, and thirdly, high velocity of recording.

This is not only true for the types of tapeto retinal degeneration mentioned above but also for any other type of degeneration e g, the amaurosis congenita Leber (Henkes and Verduin (4))

Apart from this, a combined electrodiagnostic procedure as described above, may reveal the fact that—though funduscopy seems to restrict the degenerative process to a certain area, e g, the macular

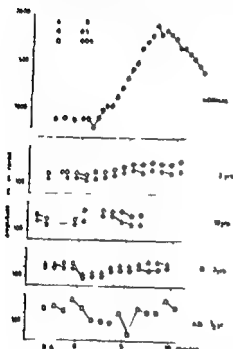


FIG. 5 EOG-curve recorded in a normal subject compared with FOG-curves recorded in narcosis. Setup described in text. Curves recorded in children P. K. and M. K. (cerebromacular degeneration) and J. B. and A. B. (X chromosomal tapetoretinal degeneration) are definitely abnormal and identical with LOG-curves found in fully developed tapeto-retinal degeneration.

region—the whole of the retinal system actually is affected. Such conditions have been encountered repeatedly in the juvenile macular degeneration. The implication of such, however, will be discussed elsewhere.

### CONCLUSIONS

1. Electro diagnostic procedures (ERG and EOG) are essential in order to ensure the diagnosis in degenerative disorders of the retina at the earliest moment possible.

2. Recording of scotopic ERG and of EOG is the procedure demonstrating at the earliest moment of alterations, even before the fundi oculi show alterations whatever. The photopic flicker ERG (photopic branch of GII curve) gives the deteriorations only at a later stage.

3. An LOG examination in narcosis is a simple procedure. Its introduction in the routine procedure of electro diagnosis of retinal disorders is worth while.

### SUMMARY

A combined electro diagnostic procedure consisting of electro-retinography and electro-oculography is advocated in the diagnosis of tapeto-retinal degenerations in the young child.



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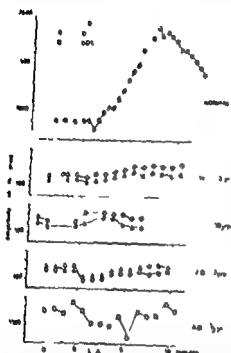


FIG. 5 LOG curve recorded in a normal subject compared with FOG-curves recorded in narcosis. Setup described in text. Curves recorded in children P.K. and M.K. (cerebromacular degeneration) and J.B. and A.B. (X-chromosomal tapetoretinal degeneration) are definitely abnormal and identical with LOG curves found in fully developed tapeto-retinal degeneration.

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## CONCLUSIONS

1. Electrodiagnostic procedures (ERG and FOG) are essential in order to ensure the diagnosis in degenerative disorders of the retina at the earliest moment possible.

2. Recording of scotopic ERG and of FOG is the procedure demonstrating at the earliest moment of alterations even before the fundi oculi show alterations whatever. The photopic flicker ERG (photopic branch of CIE curve) gives the deteriorations only at a later stage.

3. An FOG examination in narcosis is a simple procedure. Its introduction in the routine procedure of electrodiagnosis of retinal disorders is worth while.

## SUMMARY

A combined electro-diagnostic procedure consisting of electro-retinography and electro-oculography is advocated in the diagnosis of tapeto-retinal degenerations in the young child.

although, as I have already pointed out, the classical picture of Eales's disease was not reproduced. Elliot (1954, 1958) is perhaps the most enthusiastic protagonist of the tuberculous allergy theory today, and from his extensive personal experience of a large series of 55 cases would attribute all cases to this cause. He cites focal reactions in the retina after the injection of tuberculin as an indication of this aetiology, a point previously made by Werdenberg (1940) and Lang (1955). White (1961) found a high degree of cutaneous sensitivity to old tuberculin in 10 of 15 cases of retinal vasculitis.

There are two further associations which strengthen this view. First, Eales's disease has been reported in association with *sarcoidosis*, both with and without uveitis, and whatever the aetiology of sarcoidosis it surely — at least in some instances — bears a relation to tuberculosis. It is known that the sarcoid granulomatous reactions may selectively affect the retinal vessels (Gould and Kaufman, 1961; Witmer, 1948), although not producing the fundus picture of Eales's disease. Secondly, the histology of retinal vasculitis is similar to that of *erythema nodosum* (Harr, 1948) which also had a high incidence of tuberculosis, and also in sarcoidosis (Vesey and Wilkinson, 1959). It could be postulated therefore that Eales's disease is a vasculitis of the same nature as erythema nodosum, the one affecting the retinal and the other dermal vessels, while sarcoidosis is a variety of this reaction all being related through some form of tuberculous allergy.

If this were so it is remarkable that Eales's disease is so rarely associated with erythema nodosum — although the association has been recorded (Donders, 1958) — and it is surprising that Eales's disease presents so often in otherwise healthy young individuals, and, unlike erythema nodosum and sarcoidosis, is not typically associated with raised and abnormal serum globulin levels (Dodson and Pieper, 1959), nor does it show the same prompt response to cortisone therapy. These are puzzling aspects.

## OTHER INFECTIONS

If one accepts the thesis that Eales's disease is due to a tuberculous hypersensitivity then I think one must also be prepared to concede that other antigens might equally well initiate such a reaction, as originally proposed by O'Malley, (1944). The evidence in the literature certainly suggests this to be the case for retinal vasculitis has been reported in a wide variety of unrelated diseases, such as brucellosis (Puig Solanes and others, 1953; Foggitt, 1954; White, 1961), torulosis (Beck and others, 1955), infectious mononucleosis (Jones, 1954), Rickettsia (Fontana and Birnbaum, 1960), and the virus of Behçet's disease (Bouzas, 1957), syphilis (Ginnoff, 1921), leprosy (Iandru, 1961), toxoplasmosis (d'Aron, 1959), and even focal infection has been suspected (Kripp, 1935; Moffatt, 1946; Werner, 1946). Incidentally such an association with a variety of diseases due to infective or toxic agents is true also of erythema nodosum (Perry, 1944). It is interesting that all of these conditions are infections, bacterial, spirochaetal or

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## PERIODICAL VIBRATIONS ON THE ELECTROMYOGRAM OF THE EXTRAOCULAR MUSCLES

KUBOKI TETSUYA and DOMON EMI (Japan)

Since 1923 electromyography of the extraocular muscles has been one of the studies in ophthalmology. However, basic information about these particular muscles has been lacking. We will report here on some basic features of the electromyograph of these muscles, especially the internal rectus.

Fig. 1. As an electrode, a single needle electrode made of a steel wire with a diameter of 0.3 mm was applied. It was insulated with paint made of synthetic resin except for the tip. The needle usually was inserted into the muscle through the skin of the orbital margin. This slide shows the needle having been inserted to examine the internal rectus.

Fig. 2. This figure represents three patterns of the electromyograph of an extraocular muscle. The top recording shows single oscillations of a single motor unit. It is obtained with a needle electrode having a very small naked area at the tip. The middle recording shows an interference pattern, which is recorded with a needle having a relatively large naked area at the tip. The bottom recording was obtained by our own original method. This periodical wave is the result of summation of single oscillations of many motor units. The chief components of our method are firstly, relatively large naked area on the needle; secondly, some distance between the muscle and the needle; and thirdly, high velocity of recording.



FIG 1

### THREE PATTERNS OF EMG (INTERNAL RECTUS)

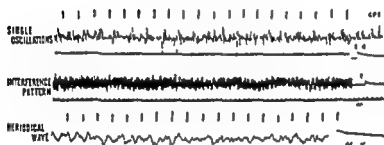


FIG 2

### INTERNAL RECTUS

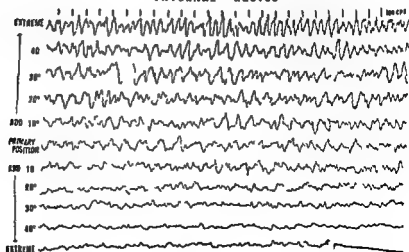


FIG 3

## EXTERNAL RECTUS

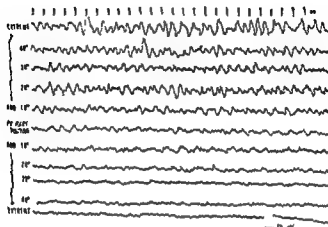


FIG. 4

## FREQUENCY DISTRIBUTION OF THE WAVE

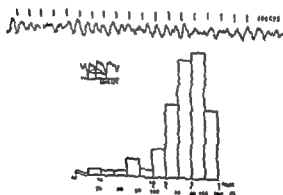


FIG. 5

Fig. 3 These recordings are the periodical waves of the internal rectus at various horizontal positions of the eye. On the recordings are observed periodical vibrations which vary in frequency with the contraction of the muscle.

Fig. 4 These waves were obtained from the external rectus. They resemble to a large extent, the waves of the internal rectus.

Fig. 5 The periodical waves were analysed by several methods. Here I present one of the practical methods. By measuring the length of each periodical wave a histogram of the frequency distribution of the waves with respect to the length or period of the waves was made.



FIG 1

### THREE PATTERNS OF EMG (INTERNAL RECTUS)

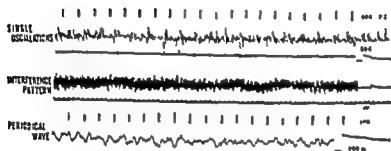


FIG 2

### INTERNAL RECTUS

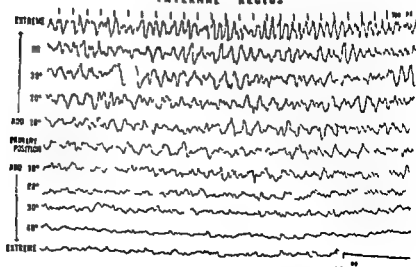


FIG 3

## EXTERNAL RECTUS

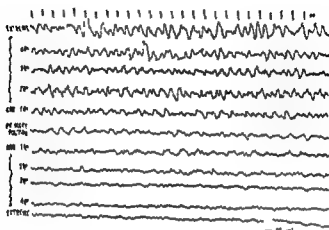


FIG 4

## FREQUENCY DISTRIBUTION OF THE WAVE

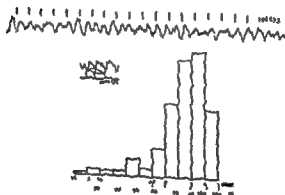


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FIG 1

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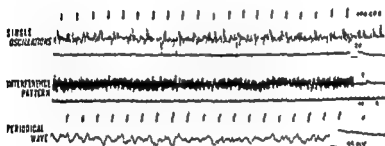


FIG 2

### INTERNAL RECTUS

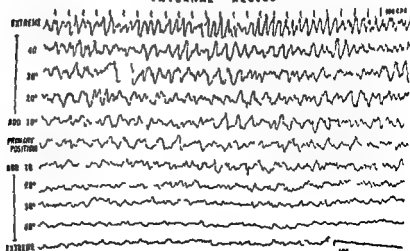


FIG 3

TONIC UNIT AND SLOW RHYTHM  
INTERNAL RECTUS

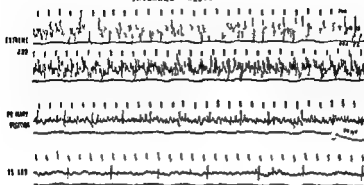


FIG 9

INTERNAL RECTUS

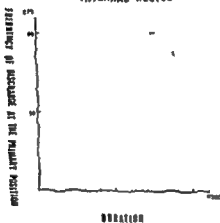


FIG 10

WAVE PATTERNS IN DISCHARGE

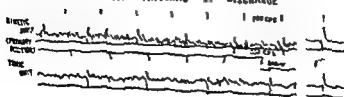


FIG 11

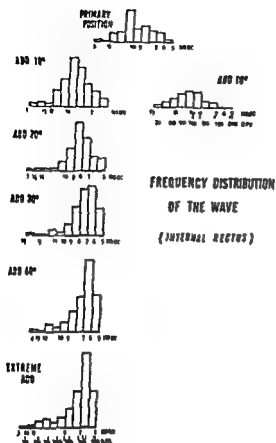


FIG 6

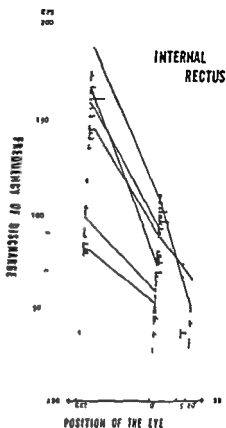


FIG 7

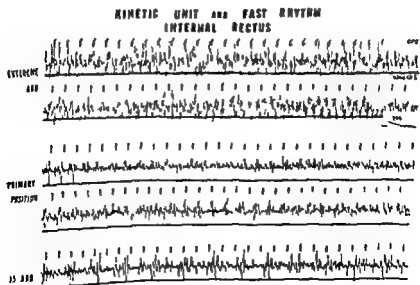


FIG 8

# TONIC UNIT AND SLOW RHYTHM INTERNAL RECTUS

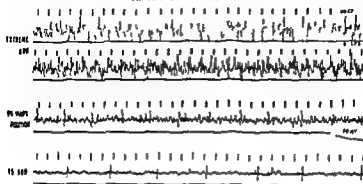


FIG 9

# INTERNAL RECTUS

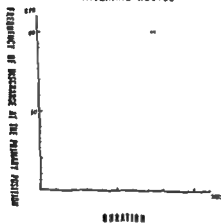


FIG 10

# WAVE PATTERNS OF DISCHARGE

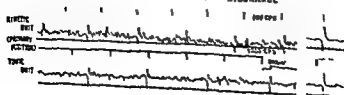


FIG 11

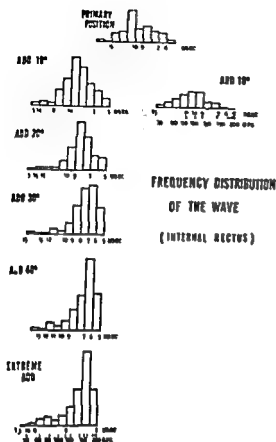


FIG 6

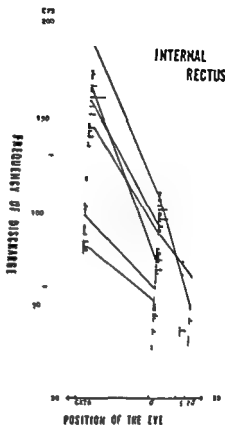


FIG 7

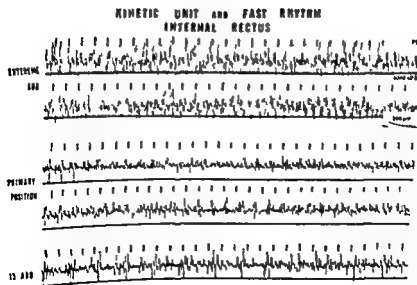


FIG 8

viral in which immune mechanisms are especially prominent and in which hypersensitivity is known to develop

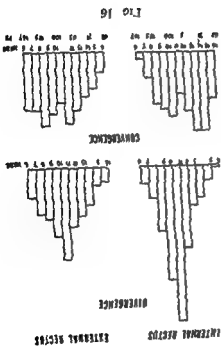
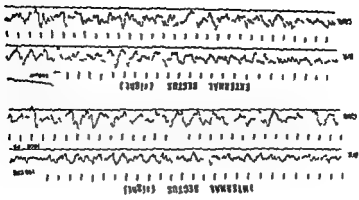
### ASSOCIATION WITH NERVOUS MANIFESTATIONS

There seems to be no doubt that retinal perivasculitis can occur in association with nervous manifestations — an incidence of 16 per cent has been quoted (Ballantyne and Michaelson 1948). The suggestion has been made that this is due to a coincidental periphlebitis of the cerebral vessels (Avenfeld, 1921, 1927, 1930) and some of the conditions reported are apoplexy (von Graefe 1854) convulsions (Ballantyne 1909), transient paralysis (Lowenstein, 1931) polyneuritis (Duvour and Bernard 1933) epilepsy (Haverkorn van Rij ewijk, 1938) paraplegia (Silfverskiöld, 1947) and severe headaches (Veirs, 1948) but most notably it has been described in association with multiple sclerosis (Ter Braak and van Herwaarden 1933 Rucker 1945, 1947, Haar 1948, 1949, 1953 Wybar, 1952 Gougard and Paris 1954 Hagedoorn 1955 Orban 1955 Paufigue and Etienne 1955 Shubova and Konchakova, 1957) in which disease retinal periphlebitis has a reported incidence varying from 10 to 40 per cent (Donders 1958).

It is questionable, however, whether many of these cases should be considered in the category of Eales's disease since predominance in the male sex was not always a feature and retinal haemorrhages and retinitis proliferans were frequently absent. Moreover as suggested by Jefferson and Cloake (1952) there is the possibility that the retinal and neurological manifestations may co-exist by chance. It is of interest that recent clinical investigations have obtained contradictory evidence. Thus Silfverskiöld (1947) reported 22 and Jefferson and Cloake (1952) six typical cases of Eales's disease showing no evidence of neurological involvement whereas White (1961) found neurological disorders in seven of 17 typical cases. Conversely Donders (1958) found no evidence of retinal vasculitis in 25 cases of multiple sclerosis whereas Scott (1961) found sheathing of the retinal veins in seven of 65 cases.

The most recent view is that of White (1961) who maintains that the association is a real one and that the retinal vasculitis is a non-specific inflammatory lesion which probably occurs in the vessels of the parenchyma and meningeal coverings of the brain and spinal cord. According to him the fact that similar lesions may develop in the central retinal vein as originally shown by Ballantyne and Michaelson (1934) and by Verhoeff and Simpson (1940) and more recently by Lyle and Wybar (1961) merely emphasises the anatomical and functional continuity between the retina and the remainder of the central nervous system.

Are we to assume then that Eales's disease is the retinal expression of a vasculitis which may affect the whole central nervous system? This is a crucial question which cannot yet be decided for it appears is often denied as supported. Francois and Neetens (1959) in describing a characteristic instance of sheathing of the retinal veins in a case of



DISCUSSION

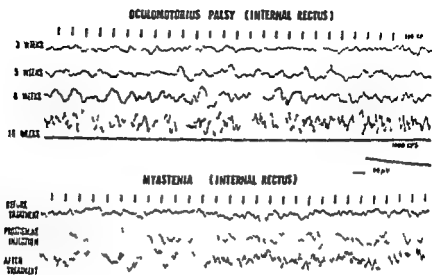


FIG 12

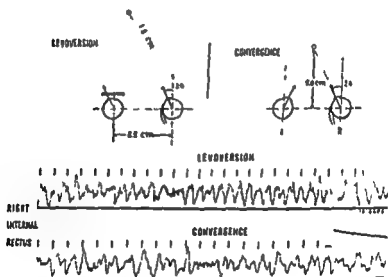


FIG 13

Fig 6 These are the frequency diagrams of the internal rectus corresponding to each horizontal position of the eye. We can know that the waves of the primary position have a periodicity of about one hundred cycles per second, which increases in frequency proportionally to the contraction of the muscle, until a maximum of 160 cycles per second is reached at extreme contraction. Furthermore, on intense contraction of the muscle, there appears another maximum on the diagrams in the region around 90 cycles per second. We designated the former the "fast rhythm", and the latter the "slow rhythm". We must now confess that this explanation concerning the relation of



Fig 8 This figure shows the single oscillations of the kinetic motor unit, which gives rise to the fast rhythm at the extreme adducted position and also at the primary position

Fig 9 These are the samples of the tonic units This kind of unit gives rise to the slow rhythm, only in the intense contraction of the muscle We don't have much data on the external rectus but it seems to resemble the internal rectus to a high degree

Fig 10 This figure represents the relation between the duration and the frequency of discharge at the primary position of a single motor unit of the internal rectus It is conceivable that the kinetic unit has a high frequency and a long duration while the tonic unit has a low frequency and a short duration

Fig 11 The upper two recordings show the samples of a kinetic unit and tonic unit

Fig 12 In a case with oculomotor palsy abnormally slow rhythm was observed during the process of recovery In a case with myasthenia very irregular patterns were observed

Fig 13 The most interesting is the wave pattern of the internal rectus upon convergence The frequency of the rhythm on the wave decreases remarkably upon convergence, although the concerned eye does not change position

Fig 14 In order to investigate both horizontal recti it is advantageous to use the position of unilateral convergence

Fig 15 The waves of both internal and external rectus muscles of the resting eye revealed a decrease in rhythm upon convergence However it is less remarkable in the external rectus

Fig 16 The frequency diagrams of the waves indicate that the predominant rhythm of both recti becomes slower upon convergence

Fig 17 This phenomenon was confirmed by observing the activity of a single motor unit This recording shows one example of a unit of the internal rectus which decreases in discharge frequency upon convergence

Fig 18 On the other hand we can find occasionally some unit showing conversely, higher activity upon convergence

Fig 19 These curves represent the changes of discharge interval of single motor units of the internal rectus Here we can find three types of unit The motor unit of the first type which decreases in frequency upon convergence, seems to belong to the kinetic group and to be the predominant one This would be related to the phenomenon that convergent movement is more limited than conjugate adduction The units of the second and the third type seem to be small in number and the relationship of them to the kinetic and tonic groups is not clear

Fig 20 Upon a divergent movement just the converse phenomenon were observed

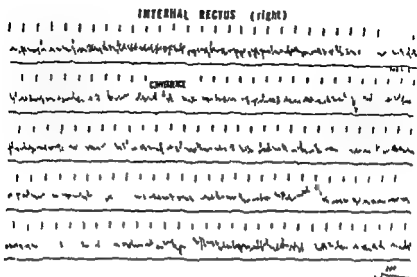


FIG 17

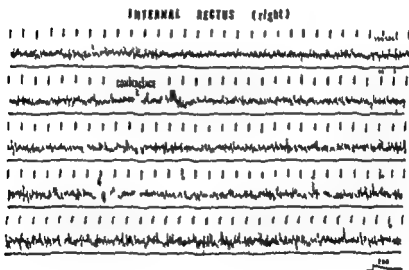


FIG 18

the two rhythms is different from the one which was written in the summary. The reason will be clarified in the following data.

Fig 7 This figure shows the frequency of discharge of single motor units of the internal rectus, in relation to the horizontal positions of the eye. From the distribution of the points at the extreme adducted position, it is inferred that the motor units of this muscle are roughly divided into two functional groups. The one group shows a frequency of discharge around 160 cycles per second while the other group around 90 cycles per second. The former group is presumed to be the origin of the fast rhythm, and the latter of the slow rhythm. We call them for convenience the 'kinetic unit' and the 'tonic unit'.

Fig 8 This figure shows the single oscillations of the kinetic motor unit, which gives rise to the fast rhythm at the extreme adducted position and also at the primary position

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## INTERNAL RECTUS

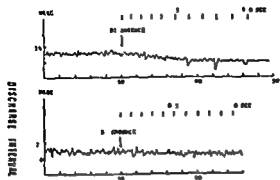


FIG 19

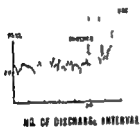
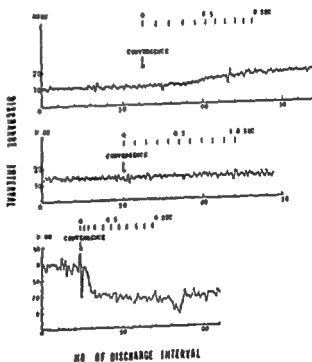


FIG 20

## INTERNAL RECTUS



## EXTERNAL RECTUS

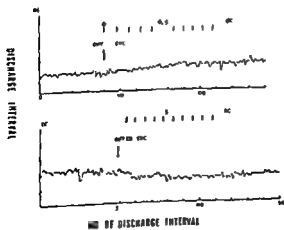


FIG 21

Fig 21 The external rectus, acted similarly to the internal rectus

In conclusion we found two functional types of motor units in the internal rectus and called them the kinetic and the tonic unit. They are respectively the origin of the fast and the slow rhythm.

Upon convergence, a decrease in frequency of the fast rhythm was observed and it was presumed that it was due to the decrease of discharge frequency of the kinetic motor units.

The external rectus greatly resembles the internal rectus; however, the details were not clear.

## INTERNAL RECTUS

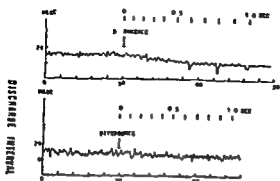


Fig 19

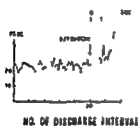
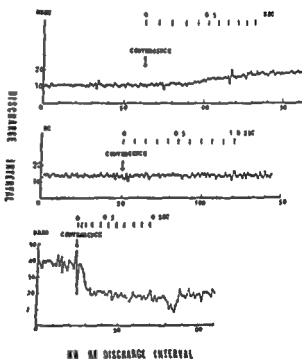


Fig 20

## INTERNAL RECTUS



## EXTERNAL RECTUS

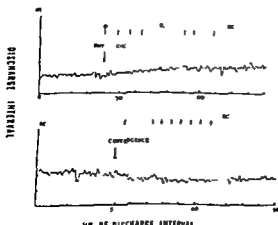


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The external rectus greatly resembles the internal rectus however, the details were not clear.





multiple sclerosis believe that this is not a true inflammatory reaction but results from the accumulation and absorption of the disintegrating products of nervous tissue. A similar suggestion was made by Greenfield (1958) in the case of multiple sclerosis, although he postulated that the perivascular infiltration was secondary to the destruction of myelin, which of course is not present in the retina, making the analogy difficult to maintain. Moreover, it should be remembered that destruction of the retina in such diseases as diabetes, or in arterial or venous occlusion is not usually accompanied by an infiltration of inflammatory cells. In fact Francois and Neetens (1959) themselves pointed out important differences between the fundus picture of Eales's disease and the sheathing of the retinal vessels in multiple sclerosis, certainly the granulomatous type of reaction occasionally seen in Eales's disease has not been described in multiple sclerosis.

Nevertheless, it is possible that the occasional co-existence of Eales's disease and multiple sclerosis may be explained on an allergic basis, for recent research into the aetiology of the demyelinating diseases is emphasizing to an increasing degree the possible role of allergic factors by invoking an auto-immune reaction to neural protein, (Krabt and others, 1941, Lerrero, 1944). The relationship is not, however, a simple one for brain tissue antigen alone is unable to produce experimental demyelination and in some way requires the assistance of infectious agents to form a complete demyelinating antigen. It has been suggested, for instance, that experimental allergic encephalitis is elicited by neural protein as an anamnestic response in a co-existing but unrelated immune state, such as may be excited by tuberculo-protein or other bacterial or viral antigen (Lumsden, 1961) and it has lately been claimed that the prominent demyelination may itself be secondary to an allergic alteration in the biochemical characters of the small venous walls (Field, 1961). Here then may lie the connection between multiple sclerosis and retinal vasculitis.

#### OTHER AETIOLOGICAL CONSIDERATIONS

The original suggestion of Marchesani (1934, b) that Eales's disease was a manifestation of thrombo-angitis obliterans (Buerger's disease) was subsequently so discredited, particularly by Schmidt (1945) who found no evidence of this disease in 25 patients with retinal periphlebitis, and no evidence of retinal changes in 86 cases of thrombo-angitis obliterans, that I think we should dismiss this possibility from consideration until more convincing, supporting evidence is forthcoming.

If we are to learn, however, from the successful solution of disease problems in the past, it may be wise to break away for a moment from the main stream of contemporary thought and to ask ourselves whether Eales's disease is in fact an inflammatory condition at all. We know, for instance, that the clinical picture of retinal sheathing may not necessarily be inflammatory and that some pathological examinations of Eales's disease have shown no inflammation - even

**SYMPOSIUM VI**

**INTERNATIONAL ORGANIZATION AGAINST  
TRACHOMA**



# INTERNATIONAL ORGANIZATION AGAINST TRACHOMA

PROF ■ B BIETTI

I am particularly happy to welcome the Colleagues that are gathered here for the occasion of the General Assembly of the International Organization Against Trachoma held parallel with the International Congress of Ophthalmology. I send a particular greeting to our hosts the Indian Ophthalmologists so active in the field of trachomatology and to the representatives of WHO whose regional office for South East Asia facilitated our presence to the actual Conference organizing the trachoma meeting just before the Congress itself.

The number and the importance of the papers to be presented gives testimony that trachoma still aroused a great deal of interest among the ophthalmologists. They are the best confirmation for the existence of our Organization which co-operates with the League Against Trachoma for the preparation and co-ordination of the scientific meetings and for the publication of the *Revue Internationale du Trachome*. The co-operation with the League and the activity of Jean Sedan as General Secretary of both Organizations, allows to enrich our international meetings with investigations which are indispensable reviews on the various chapters of trachomatology. The recent advances on the studies on trachoma opens new horizons to research and to its practical developments particularly in the fields of the problems of immunology, prophylaxis and treatment. These perspectives permit us to foresee a great interest for our future meetings.

I wish to count on your collaboration and scientific support for the future and declare officially open the activity of our General Assembly held on the occasion of the XIX International Congress of Ophthalmology.

## THE PRESENT DISTRIBUTION OF TRACHOMA IN THE WORLD

G B BIETTI, M J GREYCHE, R VOZZA

*(Report to the Meeting of the International Organization Against Trachoma, New Delhi, 1962)*

The aim of this report, which has been already published in the third number of the R I T, 1962 is not only to study the present state of the distribution of trachoma in the world, but also to analyze the factors which have contributed to the spread of the disease and the reason of the geographical differences in the clinical picture. The 200 pages of the report are divided in five chapters.

The first chapter deals with the evaluation of the possible rates of morbidity as obtained by the compulsory declaration of cases, by the evaluation of the ophthalmologists in the endemic areas, by the hospital and dispensary statistics and by the examinations of students and recruits, sometimes by "roadside" sampling. All the aforementioned methods are susceptible to criticism and could give place to data which are far from the real trichomatous index of the whole population. This can be obtained with satisfactory approximation only by means of a "sampling survey" carried out on a statistically sound sample. During the collection of data for the present report, it was noticed that the school index, once considered practically equivalent to the general one, could be much higher in relation to the widespread use of drugs active on the trachoma virus and to the increased tendency to spontaneous healing, particularly in the areas where trachoma shows a reduced diffusion and a milder course. In all the forthcoming epidemiological surveys this point should be considered, having also been recommended in the last Conference on ocular contagious disease, held in 1961 at Istanbul under the auspices of WHO.

In the following chapter (2nd) are reported the epidemiological data as obtained from documents kindly supplied by WHO, from recent papers on the subject and from personal communications of the ophthalmologists of the endemic areas.

These data, which may be only approximately summarized because of the non homogeneous diffusion within the same country, demonstrated that trachoma still maintains in the world a widespread although irregular distribution which does not differ considerably on the whole, from that reported by MacCALLAN in 1936.

The affected areas may be therefore classified as follows

- (1) Areas where the majority of the population is affected

Egypt Libya Arab Palestine, Erythrean highlands, Kuwait and some districts of Tunisia, Algeria Morocco, Syria Lebanon Iraq, Iran Saudi Arabia Northern India, Viet Nam and China

(2) Trachoma highly widespread (trachomatous index with variable rates from 20 to 50 %)

Sudan Tunisia Algeria Morocco, Syria, Lebanon Iraq Iran Jordan Aden Southern Turkey Afghanistan South Viet Nam Laos Cambodia, Continental China India (areas), Indonesia, Borneo Thailand West Pakistan, Burma Equatorial East and South Africa (among the native populations)

(3) Trachoma quite common (trachomatous index 1 to 20%)

Mediterranean coasts of Spain Portugal Southern Italy Mediterranean Islands Greece Poland Hungary, Balkan States Rumania Bulgaria Southern and Central Russia Lebanon, Central and Northern Turkey Israel India (areas) Ceylon Korea Pacific Islands, Japan Pakistan Australia (among the aborigines) United States (among the American Indians), Argentina, Brazil Mexico New Zealand (among the Maoris) West Africa

(4) Sporadic cases of trachoma

Central and Northern Italy Finland Baltic States Sweden Ireland France (imported cases only) Philippines, Chile Guatemala Honduras Panama, Paraguay, Peru Salvador, Uruguay, Venezuela U S A (non Indian populations)

(5) Trachoma practically extinct

Switzerland Austria Germany Holland, Belgium, England and Scotland Denmark Norway Iceland and Canada

The present state of distribution of trachoma demonstrates that generally decrease of the trachomatous index took place reports of its increase being mostly related to better epidemiological information.

It was observed that trachoma is in the place of extinction in Europe Infective centres are only present on the Mediterranean coasts (Spain Southern Italy Greece) and Islands (Sardinia Corsica Sicily Crete Greek Islands) in Portugal in the Balkans (Yugoslavia, Hungary) in Southern Russia

Substantial reductions of the trachomatous index were obtained among the African and Asian countries with very high contamination only in Morocco Tunisia Algeria Japan and to a lesser extent in Eritrea and South Africa

A very efficient control brought the disease to the extinction among the white population of the U S A where also the morbidity among the Indians is considerably reduced

Relying on these data an analysis was carried out in chapter 3, on the factors suitable of determining differences in the clinical picture of the disease in the world The authors have studied the influence of the

historical events which had an influence in this respect, as great migrations, military events (wars of conquest, transfers of garrisons) reasons of trade and migrations of workers

The importance of these phenomena has been discussed in detail as well as the local factors having enhancing or inhibitory activity on the spread of trachoma. These were divided as follows

- (1) Factors related to the individual,
- (2) Ecological or environmental factors,
- (3) Factors related to the properties of the infectious agent,

In the first group (factors related to the individual) the authors considered the importance of age, sex, race, origin, previous or concomitant general diseases, diet, immunitary condition (immunity and allergy), and of the preexisting or concomitant diseases of the ocular apparatus

As to the importance of the ecological or environmental factors they are considered to be of epidemiological interest, meteorological conditions, personal hygiene, habits, religious practices, cultural and social level, professions, density of population, local environment and the possible vectors of the virus

As to the last group (properties of the infectious agent) it was noticed by the AA that the isolation of trachoma virus in the 5 continents will certainly clarify the importance of this problem

At the present time however in spite of the evidence of at least two antigenic viral prototypes, the importance of this laboratory finding has not been fully evaluated

The following chapter (4th) deals with the geographical differences in the clinical picture of trachoma. The discussion of this problem is made difficult by the fact that the data referred to in the literature can hardly be compared because of the great disparity in the criteria used in the evaluation and in the collection of the clinical data

It can be stated however that, considering individually the trachoma cases, no peculiar characteristics can be found in different places

Differential geographical characteristics can be established only by taking into consideration some of the clinical features of the disease as the age of onset, the appearance of scarring, the importance of the conjunctival hypertrophy, the presence and extent of corneal involvement, the presence of trichiasis etc

A typical difficulty in comparing the data of the literature in this respect is however demonstrated when one finds it practically impossible to evaluate the data concerning the corneal pinnus since no agreement has ever been reached, even on the definition of this lesion

More reliable being less liable to errors or disparity of opinions in its evaluation, are the data relative to the incidence of entropion

trichiasis, with which it is possible to obtain an index of severity of trachoma not only geographical, but also for the same area in successive examinations

From the evaluation of this index, as well as others of the same reliability it was possible to demonstrate that the decrease of the trachomatous index is almost constantly preceded by a decrease of the incidence of complications and of disabling sequelae

From a general point of view, it was possible to conclude that the factors capable of inducing geographical differences in the clinical picture of trachoma can be grouped as follows

- (1) Age of onset,
- (2) Association with other kinds of conjunctivitis, mainly of bacterial origin,
- (3) Degree of endemicity in the area,
- (4) Hygienic habits and infectivity of the individual environment,
- (5) Climatic factors,
- (6) Properties of the viral agent
- (7) Economical and social factors
- (8) Therapeutic treatments carried out in the area
- (9) Race
- (10) Mode of transmission

Out of the aforementioned factors particularly important are believed to be the age of onset and the degree of endemicity which are however likely to influence each other. Equally important are the incidence of bacterial superimposition and the socio-economic conditions of the environment. Although it can not be ruled out, the influence of the race is now considered with less attention

It should be noted however, that all the aforementioned factors cannot be considered singularly in their activity since they are frequently present at the same time in the area and they tend to influence each other in giving place to the particular features of the disease in a certain district

As to the distribution of the blindness due to trachoma the following conclusions were reached

- (1) The incidence of blindness is directly proportional to the level of endemicity
- (2) No racial groups are spared by the blindness that result from trachoma
- (3) The incidence of blindness is conditioned not only by the degree of contamination of the area but also by the activity of the same factors which are capable of rising the severity of the disease like bacterial infection, socio-economic, under-development etc.



In the last chapter (5th) an analysis of the *causes of the decrease of the trachomatous index* in certain districts, was carried out

This problem was studied in the countries where reliable data on the prevalence of trachoma were available for the last 60 years, i.e. the European countries, the U.S.A. and Japan

A particular attention was devoted to the evolution in the behaviour of the disease in Italy where in this period trachoma was brought to extinction in the Central and Northern districts, while a considerable number of cases are still present in the South and Islands. This different diffusion was related to the mass and school campaigns regularly carried out during this period and to the considerable improvement in the standard of living. This phenomenon, particularly evident in the Central and Northern districts, undoubtedly contributed considerably to the decreases of the trachomatous index

# EFFECT OF TRACHOMA WITH LEDERKYN ACETYL INTRAMUSCULARLY INJECTED

TOSHIO KISHIDA

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The structure of Lederkyn Acetyl, 3 (N 1 Acetylsulfanilamido) 6 methoxypyridazine is as figure 1. This compound was the outcome of the research conducted by Medical Research of Lederle Laboratories Pearl River New York in 1958. This medicine belongs to one of the repository (slowly absorbed or slowly eliminated) substances which show an intensive inhibitive effect not only to streptococcus, staphylococcus, pneumococcus, meningococcus, gonococcus, colibacillus, dysentery bacillus, proteus vulgaris but also to sulfareistant viruses.

According to the reports of Bietti (1959) and Wong (1961) Lederkyn used orally has given excellent results in the treatment of trachoma. Lederkyn Acetyl is the 25 % suspension which can be applied intramuscularly. This new medicine was kindly put at our disposal by Lederle Laboratories. Our experiment is carried out on ten trachoma patients whose results and side effects are reported as under.

## MATERIALS AND METHODS

Ten trachoma patients, three men and seven women, ranging in age from 14 to 48 and in weight from 40 to 56 kg., were given intramuscularly 5 to 7 times at intervals of 7 days. The severity of trachoma was all mild, being Tr I to Tr IIb under the McCallan classification.

## RESULTS

Course of the trachoma symptoms. Decrease in conjunctival hyperemia was observable after the administration of the third injection and was still more remarkable after the fifth injection. From about this time onward papillae and follicles were evidently on the decrease. One month after the last injection pronounced improvement on the conjunctival findings were evident with papillary hypertrophy and formation of follicles left in almost none of the cases though in only one case a mild degree of papillary hypertrophy was still to be noted as shown in table 1. However this case was also completely cured in three months. Improvement was less impressive against the pannus. Twenty clinical findings before and after treatment are shown in figures 2 to 21. Scarcely any side effect was observed following intra

muscular administration of Federlyn Acetyl. The renal function observed by 17-KS in urine before and after the injection is shown in figure 22. As in the figure there were no impaired symptoms. There was no variation in serum sodium and calcium levels as shown in figures 23 and 24. There was neither variation of the number of erythrocytes

TABLE 1—*Course of Trachoma Symptoms after Injections*

Case No and Stage	Initial Findings	At the 3rd Injection	One Month after the Last Injection
1 Ir III	Conjunctival hyperemia (+) Papillary hypertrophy (+) Conjunctival scar (+) Pannus (+)	(→) (→) (+) (+)	(-) (-) (+) (+)
2 Ir I	Conjunctival hyperemia (+) Conjunctival hypertrophy (-)	(→) (→)	(-) (-)
3 Ir IIb	Papillary hypertrophy (+) Conjunctival hyperemia (+)	(+) (→)	(+) (-)
4 Tr IIb	Conjunctival hyperemia (+) Papillary hypertrophy (+)	(→) (→)	(-) (-)
5 Ir IIb	Conjunctival hyperemia (+) Papillary hypertrophy (+) Pannus (+)	(→) (→) (+)	(-) (+) (-)
6 Ir IIb	Conjunctival hyperemia (+) Conjunctival hypertrophy (+) Papillary hypertrophy (+)	(→) (+) (→)	(+) (-) (-)
7 Ir III	Conjunctival hyperemia (+) Papillary hypertrophy (+) Conjunctival hypertrophy (+) Conjunctival scar (+) Pannus (+)	(-) (+) (+) (+) (+)	(-) (-) (+) (-) (-)
8 Ir IIb	Conjunctival hyperemia (+) Papillary hypertrophy (+) Pannus (+)	(-) (→) (+)	(-) (+) (-)
9 Ir IIb	Conjunctival hyperemia (+) Papillary hypertrophy (+) Pannus (+)	(→) (+) (+)	(-) (-) (+)
10 Tr III	Conjunctival hyperemia (+) Papillary hypertrophy (+)	(-) (→)	(-) (+)

Remarks (+) Positive reaction  
(→) Decrease  
(-) Disappearance

in the early stages (Elliott, 1954). Pathologically, retinal perivasculitis is seen very commonly, yet Eales's disease is rare by comparison which makes one a little suspicious of there being any relationship.

There have in fact been several suggestions that Eales's disease may not have an inflammatory cause. French workers have particularly emphasized the role of endocrine factors (Mawas and Herschberg 1953) and others have pointed to defects in the haemopoietic system, such as anaemia (Cohen 1924, Rollet, 1930) hypoprolthrombinaemia (Mawas 1945) or hyperthrombinaemia (Donner, 1953) polycythaemia (Litauer and Januszewski 1934) or to some undiscussed blood deficiency (Hutchinson 1932), while a deficiency of essential fatty acids (Sinclair, 1956) or of Vitamin C (Zwiazner and others 1948) have been suggested.

In recent years it has become apparent that peripheral lesions in the retina can result from entirely non-inflammatory conditions which are all in some way attributable to circulatory embarrassment in the retina. Peripheral haemorrhages for instance may occur in macroglobulinaemia from increased blood viscosity, haemorrhages and neovascularization may develop in pulseless disease due to retinal hypotension and Eales's disease may be closely mimicked in sickle cell haemoglobin C disease as a result of chronic and recurrent vascular occlusion (Henry and Chapman 1954, Hannon 1956, Lieb 1957, Goodman and others, 1957).

None of these suggestions however has much support at the present time. Kimura and others (1956) found no evidence of Vitamin C deficiency nor of hypoprolthrombinaemia while electrophoretic analysis of the blood plasma showed no abnormal protein pattern. Dodson and Pieper (1959) carried out an electrophoretic study of the blood proteins in 94 cases of retinal periphlebitis and found no abnormality, whereas patients with multiple sclerosis showed frequent disturbances of the protein fraction. Seidel (1955) could find no abnormality in the number and behaviour of the blood cells or in the coagulation processes and was thus unable to confirm the findings of Donner (1953) of a raised haemoglobin and erythrocyte value. Lastly it should be noted that no microscopical evidence of an inflammatory vasculitis has been found in macroglobulinaemia or sickle cell haemoglobin C disease so that a non-inflammatory concept of Eales's disease is at the moment untenable.

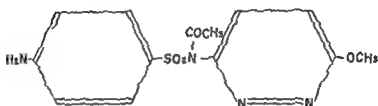
## CONCLUSION

Our knowledge of the pathology of Eales's disease does not permit any final expression of opinion on its pathogenesis or aetiology but it may be generally agreed that retinal vasculitis particularly affecting the veins is probably the initial lesion.

Vasculitis is a common pathological reaction in the retina and while in some cases the injury to the vessel walls may be due to the direct action of chemical or other toxic substances the majority are

as shown in figure 25. However, leukopenia was observed slightly by 4.8% to 25.7% as shown in figure 26.

Fig 1 Structure of Lederkyn Acetyl



3 (N-Acetylsulfonitrimido)-6-methoxypyridazine

Effect on Whole Body after Lederkyn Acetyl Intramuscularly Injected

Fig 22 17-KS in Urine

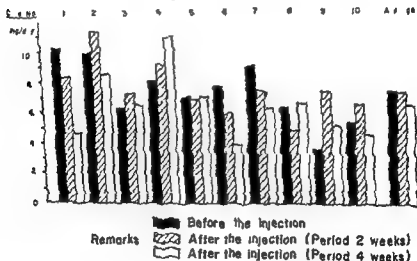
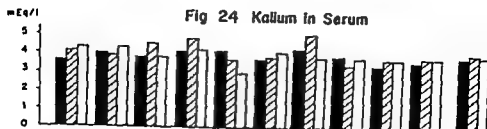
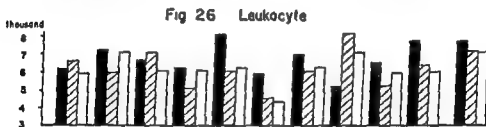
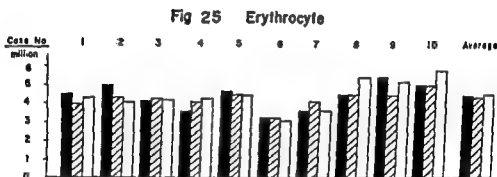


Fig 23 Sodium in Serum





See legend to Fig 22 for description



See legend to Fig 22 for description

## SUMMARY AND CONCLUSION

Lederkyn Acetyl intramuscularly injected has been established to give excellent effect in relieving mild trachoma. Five doses of 6 cc at intervals of 7 days, have been proven sufficient. There is no side effect upon the whole body. Only leukopenia by 4.8% to 26.7% was noted in 3 cases.

I wish to express my appreciation to Dr. Ottavio, Director of Lederle Laboratories, Pearl River, New York, by whom this paper was supported.

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# THE COLLAR BUTTON ' TECHNIQUE OF LID REPAIR

SIDNLY, A FOX, M D

*New York--US 4*

Basal cell epitheliomata which do not involve the lid margin are usually handled by simple skin resection, sometimes the subjacent muscle is also taken. However, once the margin or margin cum conjunctiva has become involved no matter how little it is customary to do a full thickness lid resection of the whole lesion. This has always seemed a waste since the pathologic report in most cases shows no tarsal involvement.

I should therefore like to present to you a new technique for the repair of lid epitheliomata which involve the lid margin or margin cum conjunctiva.

This technique is based on two observations.

1 The first observation is clinical. Lid epitheliomata especially the basal cell usually start below the lid margin then spread slowly downward and upward to involve the margin and conjunctiva. In a large percentage of these cases the marginal and conjunctival involvement is much less than that of the skin. Thus in a series of 91 cases of basal cell epitheliomata 39 cases showed marginal involvement and 14 also had conjunctival involvement. The area of border and conjunctival involvement was considerably less than that of the skin.

2 The second observation is pathological. Serial sections of the lesions showed most or all of the skin layers involved. The orbicularis was only rarely involved and then only in old long neglected cases. No tarsal invasion was noted in any case even where the margin and conjunctiva were invaded. This is not to say that it doesn't happen. It probably does but if so it must be rare.

One would think that the meibomian gland openings offer ready access to tarsal invasion by marginal neoplasms but this is not the case as repeated pathologic studies have shown.

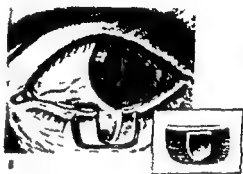
Based on these two observations the following technique of resection was evolved.

Starting at the lid margin an incision is made through skin and muscle all around the skin lesion including 2 or 3 mm of healthy tissue. Then starting at the margin again 3 mm to each side of the involved marginal (and conjunctival if involved) area two vertical incisions are made downward through tarsoconjunctiva. These incisions

are curved in to meet each other below the tarsus in healthy conjunctiva. The ends of the skin muscle and tarsoconjunctival incisions at the border are united by incisions through the gray line (Fig 1). The tissue thus outlined containing the whole lesion, the larger skin lesion and lesser marginal and conjunctival lesion, is split away from the rest of the lid en bloc (Fig B).



A



B

#### Diagram of halving by collar button resection technique

FIG A Lines of incision around lesion. Dotted lines enclose tarsoconjunctival portion of lesion

FIG B Diagram of dehiscence left when the collar button shaped section (inset) is removed

Since the amount of skin muscle resected is always much more than tarsoconjunctiva, the resected portion resembles an old fashioned collar button and hence the name (Fig B). Many variations of this technique are possible of which a few are described.

1. A medium sized lesion involving the center of the lid corrected by a horizontal tarsoconjunctival closure and vertical skin muscle flap.

In such a case a collar button resection is done as previously shown. With the help of canthotomy and cantholysis the tarsoconjunctiva is closed in the usual fashion.

Since the tumor is a shallow one, it is possible in such a case to fashion a vertical sliding skin flap, which is drawn up and sutured to the lid margin.

And here is a pathologic section through the centre of the lesion showing no tarsal involvement (Fig C).

2. In the case of a medium sized lesion at the canthus another variation in technique is possible.

Here repair is attained by means of horizontal closure of the tarsoconjunctiva as in the previous case. But the skin muscle lamina is closed by a temporal sliding flap thus taking advantage of the lesion's position. After a collar-button resection of the lesion a canthotomy and cantholysis permit closure of the tarsoconjunctiva.





FIG C Section through lesion of lid showing non invasion of tarsal glands

A temporal sliding flap is then fashioned which is pulled over the bared tarsus and sutured

Here again pathologic section showed no involvement of the tarsus

3 And finally when the lesion is large repair may be attained by a free whole skin graft

This lesion is resected collar button fashion and the tarso conjunctiva closed as in the two previous cases A free graft is taken from the ipsilateral upper lid and used to cover the dehiscence

The pathologic section shows involvement of the skin and muscle but the tarsus remained clear

#### DISCUSSION

In summary the collar button technique is suggested for (1) epitheliomata of the lid which (2) involves the lid margin or margin cum-conjunctiva and in which (3) the skin involvement is much greater than that of the margin (and conjunctiva) Wheeler pointed out long ago that the tarsus is a low grade tissue which heals poorly Perhaps this also accounts for its failure to be involved in neoplasms But however the case replacement of this inelastic relatively avascular tissue is not always easily accomplished Any procedure therefore, which minimizes tarsal loss facilitates lid repair Since the collar button technique reduces the amount of tarsal resection considerably one is frequently enabled to close the tarsoconjunctival wound directly thus avoiding tarsal grafting if one were to use the usual old techniques

Of course this technique will not be used in old neglected lesions in which the tarsus may be involved Also it is important to make sure that there has been complete excision of the neoplasm This is not difficult if sufficient healthy tissue is taken all around as described previously Furthermore this is always ascertainable by frozen section

are curved in to meet each other below the tarsus in healthy conjunctiva. The ends of the skin muscle and tarsoconjunctival incisions at the border are united by incisions through the gray line (Fig 4). The tissue thus outlined containing the whole lesion, the larger skin lesion and lesser marginal and conjunctival lesion, is split away from the rest of the lid en bloc (Fig B).



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A



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## BOUTON D'ORIENT SIMULANT UNE DACRYOCYSTITE

### A MOTOLESE

Deux raisons importantes nous ont poussé à publier l'histoire de ce cas clinique, et tout d'abord la difficulté du diagnostic qui retardait considérablement l'institution d'un traitement adéquat, puis aussi la rareté, voire la singularité, de ce cas dans notre région (Sud Est de l'Italie), jusqu'ici considérée zone exempte de maladies tropicales

#### DESCRIPTION DU CAS

I O, de Trente (Italie) — femme de 60 ans, mariée à un officier de marine

Six ans auparavant son oeil gauche s'étant mis à larmoyer, la patiente avait été soumise à de fréquents vains qu'inutiles sondages du canal lacrymal

Plus tard une dacryocystectomie. Après l'opération la cicatrice resta granuleuse en dépit de l'application de traitements variés

C'est dans ces conditions que la patiente se présenta à notre observation en septembre 1960

#### EXAMEN OBJECTIF

O D = normal en toutes ses parties

O G = bulbe oculaire normal en toutes ses parties. Dans la région du sac lacrymal une zone de tumeur plus foncée, d'aspect granuleux et semée de petites croûtes de sang. Le tout à la forme et les dimensions d'une grosse mûre à pointe tournée vers le bas limitée par la paupière supérieure vers le haut et par la partie latérale du nez vers le bord droit. le pôle inférieur atteint presque la pommette gauche



due to an allergic reaction involving a wide variety of antigens. The vessels may become sensitized through an intraocular antigenic source (lens protein, uveitis) or from an extraocular source (pulmonary tuberculosis, brucellosis), or possibly from the formation of complex autoantibodies as in multiple sclerosis.

Eales's disease is one clinical form of retinal vasculitis, usually of unknown aetiology and characterised by recurrent peripheral haemorrhages in young males. The two terms of Eales's disease and retinal vasculitis should not be used synonymously. Regarded in this way it is not surprising that Eales's disease may have multiple causes or that it should sometimes present with vasculitis elsewhere in the retina or nervous system or with other allergic manifestations in the uvea or in the body generally.

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La palpation revele une consistance molle elastique

Le bord de cette formation, assez net vers l'exterieur, est irregulier vers l'interieur et legèrement detache du fond a pic. Le tout peut etre assez facilement déplacé sur les plans profonds, malgre l'opération precedemment subie

Frottée avec un tampon la surface s'effrite par petits fragments squameux et le fond, mis à nu, saigne en nappe

Une palpation plus energique provoque l'ecoulement d'une bonne quantite d'un liquide muco-séro sanguinolent

Il est a remarquer toutefois que toutes les manœuvres auxquelles la lesion a ete soumise n'ont jamais provoque aucune douleur chez la patiente

### EVOLUTION

On décide de proceder à une nouvelle demolition du sac lacrymal et, par la meme occasion de prelever un fragment de tissu en vue d'un examen histologique car nous avons déjà emis l'hypothese d'une affection chronique specifique dont il restait encore à determiner l'agent

Avant l'operation on preleve aussi en toute asepsie une goutte de la sécrétion du fond de la lesion on en fait un frottis que l'on colore au Giemsa

La dacryocystectomie revele la presence d'un sac assez bien reforme et pourvu de pericyste presque normal

L'evolution successive est caracterisee par une premiere phase de cicatrisation apparente rapide apres laquelle la region du sac reprend son aspect primitif et l'ulceration de la plaie operatoire s'etend derechef en tous sens jusqu'a regagner es anciennes limites et presente les memes caracteristiques morphologiques que la lesion precedente

Entre temps un fragment de tissu préleve au cours de l'operation ainsi que notre frottis coloré avaient été envoyés au Laboratoire d'histologie de la Section d'anatomie et histologie pathologiques dirigée par le Prof. Dr Garau à l'Hopital provincial de Brindisi

Enfin voici le rapport que nous avons reçu du Laboratoire

### BIOPSIE N° 2267

*Détails techniques* fixation à l'alcool inclusion dans la paraffine coloration hematoxyline eosine van Gieson

*Histologie* fragment de peau à épiderme d'épaisseur irreguliere presence de tissu granuleux dispose de prevalence en ilots. Les ilots sont formes d'éléments epithelioides grands ou petits, auxquels se joignent des cellules géantes aux caracteres semblables tantot à des cellules de Langhans tantot à des cellules géantes de nature irritative

*Diagnostic histo pathologique* tissu granuleux rappelant le tissu tuberculeux (Bouton d'Orient)



## BOUTON D'ORIENT SIMULANT UNE DACRYOCYSTITE

A. MOTOLFE

Deux raisons importantes nous ont poussé à publier l'histoire de ce cas clinique, et tout d'abord la difficulté du diagnostic qui retarderait passablement l'institution d'un traitement adéquat, puis aussi la rareté, voire la singularité, de ce cas dans notre région (Sud Est de l'Italie), jusqu'ici considérée zone exempte de maladies tropicales.

### DESCRIPTION DU CAS

F O, de Tarente (Italie) — femme de 60 ans, mariée à un officier de marine.

Six ans auparavant son oeil gauche s'étant mis à larmoyer, la patiente avait été soumise à de fréquents vains et inutiles sondages du canal lacrymal.

Plus tard une dacryocystectomie. Après l'opération la cicatrice resta granuleuse en dépit de l'application de traitements variés.

C'est dans ces conditions que la patiente se présente à notre observation en septembre 1960.

### EXAMEN OBJECTIF

O D = normal en toutes ses parties.

O G = bulbe oculaire normal en toutes ses parties. Dans la région du sac lacrymal une zone de teinte plus foncée, d'aspect granuleux et semée de petites croûtes de sang. Le tout à la forme et les dimensions d'une grosse amande à pointe tournée vers le bas, limitée par la paupière supérieure vers le haut et par la partie latérale du nez vers le bord droit. Le pôle inférieur atteint presque la pommette gauche.



## (PERGOLA)

Les lésions du lupus peuvent aussi présenter des caractères analogues. Il faut alors se souvenir que leur évolution est bien plus lente que celle du Bouton d'Orient de plus si l'on appuie d'une lamelle de verre, sur la peau envahie par le lupus on voit apparaître des taches et des stries dont la teinte rappelle la couleur de la marmelade de pommes.

## (AGNELLO)

Certains caractères peuvent aussi faire prendre le Bouton d'Orient pour le *veroderma pigmentosum* surtout dans la période de l'évolution cancéreuse de ce dernier car c'est à ce moment que l'on trouve des formations verruqueuses avec érosion plus ou moins ulcérées. Mais dans ce cas aussi l'anamnèse l'évolution ainsi que les caractères morphologiques plus particuliers nous portent vers une juste différenciation.

Dans la littérature nous trouvons aussi des cas de Bouton d'Orient qui par leurs caractères morphologiques rappellent les verrues ou les chéloïdes. Parmi les cas décrits par BLHDJET il y en a qui simulaient le lupus pernio l'hémangiome et la tuberculose ulcéreuse.

HIGOUMENAKIS dresse une liste très claire des multiples aspects cliniques présentes par le Bouton d'Orient et qui peuvent le faire facilement prendre pour un impetigo un lupus une forme de tbc cutanée ou même pour une affection verruqueuse érysypeloïde furonculaire etc.

MONACELLI décrit encore d'autres formes cliniques atypiques du Bouton d'Orient rappelant surtout le lupus pernio et le lupus tumidus.

MORETTI parle d'un cas dont le tableau clinique simulait une affection épithélio-mateuse.

Quant au diagnostic différentiel entre le Bouton d'Orient et un processus cancéreux c'est encore l'examen histologique d'un fragment de tissu qui sera le plus utile sans négliger l'inoculation d'un fragment sous la peau ou dans l'œil d'un animal de laboratoire.

D'autres parties caractères d'une manifestation mycosique peuvent être pris par certains détails pour un Bouton d'Orient car il n'est pas rare de trouver dans une affection mycosique un nodule arrondi et proéminent souvent ulcéré entouré d'une zone d'infiltration pale, pourtant dans ces cas aussi un examen bactériologique nous permettra d'isoler le champignon en cause. Le laboratoire est en effet d'une extrême utilité pour arriver à une exacte différenciation de diagnostic au moyen de la recherche des micro-organismes ou des éléments spécifiques dans les produits de sécrétion de l'ulcère. Souvent à la recherche bactériologique il faut encore ajouter l'examen histologique d'un fragment prélevé à la lésion ainsi que l'inoculation de celui-ci sous la peau ou dans l'œil d'un animal de laboratoire.

Le resultat de l'examen du frottis etait le suivant on remarque la presence de corpuscules ovoides ou spheriques de 1' a 2 microns de diametre, entoures d'une mince membrane, protoplasme hyalin colore en bleu pale sans vacuoles, noyau excentrique colore en rouge

*Conclusions* Leishmaniasis tropica ou corpuscules de Wright

A la suite de ces constatations un traitement au Stibosan (antistibic) a ete immediatement institue a raison d'une ampoule de 5 cc deposee 1 m tous les trois jours. En depit d'une certaine intolerance au medicament (quelques modiques manifestations d'intoxication), le traitement a pu etre prolonge pendant deux mois environ

La derniere fois que nous avons revu cette patiente — deux mois apres le debut du traitement — la lesion etait nettement en bonne voie de guerison et ne presentait plus qu'une petite ulceration centrale entouree d'une vaste zone de reepithelialisation a bords minces et plis

#### PERGOLA DIT QUE

Objectivement parlant du point de vue de la clinique et d'apres ses caracteristiques macroscopiques, le Bouton d'Orient peut fort bien se preter comme sujet de discussion quant au diagnostic differentiel entre des affections de nature differentes et l'on pourrait aussi, comme dans le cas ci dessus, se poser la question si l'on s'agit d'un processus de neoformation d'origine inflammatoire ou d'origine neoplasique, ou bien d'une manifestation mycosique

Pour le diagnostic differentiel il faut se souvenir que parmi les nombreux processus inflammatoires se trouvent en premier lieu les processus chroniques specifiques syphilis et tbc. La syphilis, notemment, peut provoquer des ulcerations et meme des gommages comparables, a certains moments du moins, aux lesions dues au Bouton d'Orient. Toutefois les caracteristiques essentielles de l'ulcere syphilitique sont en premier lieu son evolution rapide, puis l'aspect particulier des bords et de la base et surtout l'adenopathie qui accompagne constamment cette affection. L'engorgement des ganglions precervicaux et sous-maillaires est, en effet, constant dans la syphilis tandis que l'on ne trouve presque jamais cette manifestation dans le Bouton d'Orient

Au cas ou l'on serait tente a soupconner une manifestation tuberculeuse la clinique pourra toujours, par exclusion, fournir de precieuses indications. Dans l'ulcere tbc il n'est pas rare de trouver de veritables granulations miliaires et, plus frequemment, de petits nids blanchatres caseux et des ulcerations parfois tres profondes et penetrantes qui detruisent rapidement une grande partie des tissus profonds. Il est vrai que certains de ces caracteres cliniques se retrouvent meme dans le Bouton d'Orient, mais la lenteur de l'evolution de ce dernier est toujours la pour nous mettre en garde quant a la veritable nature de l'affection

**(PERGOLA)**

Les lésions du lupus peuvent aussi présenter des caractères analogues. Il faut alors se souvenir que leur évolution est bien plus lente que celle du Bouton d'Orient, de plus si l'on appuie d'une lamelle de verre sur la peau envahie par le lupus on voit apparaître des taches et des stries dont la teinte rappelle la couleur de la marmelade de pommes.

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HIGOU MENAKIS dresse une liste très claire des multiples aspects cliniques présentés par le Bouton d'Orient et qui peuvent le faire facilement prendre pour un impetigo, un lupus, une forme de l'eczéma ou même pour une affection verruqueuse, érysipéle, furonculose, etc.

MONACHELLI décrit encore d'autres formes cliniques atypiques de Bouton d'Orient rappelant surtout le lupus, le pyoderme et le lupus.

MORFETTI parle d'un cas dont le tableau clinique simulait une affection épithélio-mateuse.

Quant au diagnostic différentiel entre le Bouton d'Orient et un processus cancéreux c'est encore l'examen histologique d'un fragment de tissu qui sera le plus utile sans négliger l'inoculation d'un fragment sous la peau ou dans l'œil d'un animal de laboratoire.

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Le résultat de l'examen du frottis était le suivant : on remarquait la présence de corpuscules ovoides ou sphériques de 1' à 2 microns de diamètre, entourés d'une mince membrane, protoplasma hyalin colore en bleu pâle sans vacuoles, noyau excentrique colore en rouge.

*Conclusions* : L'ishmanu tropical ou corpuscules de Wright

À la suite de ces constatations un traitement au Stibosan (forme stable) a été immédiatement institué à raison d'une ampoule de 5 cc déposé tous les trois jours. Il n'y eut d'une certaine intolérance au médicament (quelques modiques manifestations d'intoxication), le traitement a pu être prolongé pendant deux mois environ.

La dernière fois que nous avons revu cette patiente — deux mois après le début du traitement — la lésion était nettement en bonne voie de guérison et ne présentait plus qu'une petite ulcération centrale entourée d'une vaste zone de repigmentation à bord minces et plats.

#### PERGOLA DIT QUE

Objectivement parlant du point de vue de la clinique et d'après ses caractéristiques microscopiques, le Bouton d'Orient peut fort bien se prêter comme sujet de discussion quant au diagnostic différentiel entre des affections de nature différentes et l'on pourrait aussi, comme dans le cas ci-dessus, se poser la question si il s'agit d'un processus de neoformation d'origine inflammatoire ou d'origine néoplasique, ou bien d'une manifestation mycosique.

Pour le diagnostic différentiel il faut se souvenir que parmi les nombreux processus inflammatoires se trouvent en premier lieu les processus chroniques spécifiques : syphilis et tbc. La syphilis, notamment, peut provoquer des ulcérations et même des gommes comparables, à certains moments du moins aux lésions dues au Bouton d'Orient. Toutefois les caractéristiques essentielles de l'ulcère syphilitique sont en premier lieu son évolution rapide, puis l'aspect particulièrement des bords et de la base et surtout l'adenopathie qui accompagne constamment cette affection. L'engorgement des ganglions préauriculaires et sous-maillaires est en effet, constant dans la syphilis tandis que l'on ne trouve presque jamais cette manifestation dans le Bouton d'Orient.

Au cas où l'on se voit porté à soupçonner une manifestation tuberculeuse, la clinique pourra toujours, par exclusion, fournir de précieuses indications. Dans l'ulcère tbc il n'est pas rare de trouver de véritables granulations miliaires et, plus fréquemment, de petits îlots blanchâtres crêpeux et des ulcérations parfois très profondes et pénétrantes qui détruisent rapidement une grande partie des tissus profonds. Il est vrai que certains de ces caractères cliniques se retrouvent même dans la Bouton d'Orient, mais la lenteur de l'évolution de ce dernier est toujours là pour nous mettre en garde quant à la véritable nature de l'affection.

## RESECTION OF ORBICULARIS NERVE SUPPLY FOR INTRACTABLE BLEPHAROSPASM

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In 1931 Sidney Fox described an operation for intractable blepharospasm consisting of removal of most of the orbicularis muscle. His plan was used on the first patient who consulted us because of blepharospasm which had developed in part from repeated, excessive blinking from keratitis sicca and in part from having a highly nervous temperament.

We removed part of the orbital orbicularis most of the preseptal part and some of the pretarsal part of the orbicularis muscle. As the operation proceeded with the extensive removal of muscle tissue we feared that postoperatively the eye lids might not close but this fear was unjustified. Though the blink mechanism was still active the amplitude and intensity of the sphincter action of the orbicularis muscles was reduced to a more normal level and the patient was benefitted.

This massive removal of the orbicularis muscle was accompanied by oozing of blood from the muscle tissue and occasional spurtings of the vessels required so much time and effort that we sought an easier way to improve such patients. We then realized that if a sector of the lateral edge of the orbicularis was removed so that the nerve supply was partly disconnected that improvement might be achieved with less trauma to the patient and less effort by the surgeon.

Our second patient with intractable blepharospasm developed this condition in part because of extreme photophobia from a slowly developing incipient cataract and he too had a highly nervous temperament.

The technique About 8 to 10 cc of Xylocaine (R) Wydase (R) and epinephrine are injected along the antero-lateral angle of the face approximately 1 cm posterior to the canthal angle extending downwards vertically from the posterior edge of the eyebrow to the lower edge of the zygomatic bone.

Fig 1) A curvilinear incision is made over the posterior lateral orbicularis border and a sector about 10 mm wide and 40 to 45 mm long of the muscle is excised exposing the periosteum beneath. In severe cases a wider and longer sector of the orbicularis can be safely removed in one of our patients we removed all of the orbicularis lateral to a vertical line drawn through the lateral palpebral tendon.

Il ne faut pourtant pas oublier que le seul fait de ne pas avoir trouvé de micro organismes ne prouve pas nécessairement que l'affection ne soit pas spécifique. Dans le cas que nous venons de décrire, la recherche du parasite a été assez laborieuse justement à cause des nombreux traitements et manipulations auxquels notre patiente a été soumise, bien que les caractères morphologiques de l'affection cutanée et la présence de macrophages dans le frottis eussent dû suffire à eux seuls à confirmer le diagnostic clinique. Il faut, toutefois, être circonspect et avoir toujours recours au diagnostic différentiel dans les cas où l'examen bactériologique serait négatif.

#### RESUME

*Description d'un cas de Bouton d'Orient dans la région du sac lacrymal gauche.*

Ce cas, déjà intéressant à cause de sa rareté, est le premier cas de leishmaniose cutanée de la région du sac lacrymal qui ait été jamais observé dans le Sud Est de l'Italie.

La grande variété de tableaux cliniques présentes par la Leishmaniose accroît encore l'intérêt de ce cas au point de vue du diagnostic différentiel entre les nombreuses neo formations chroniques de nature spécifique.

Le diagnostic clinique a été confirmé par les résultats de la biopsie et des examens bactériologiques.

The skin can be united with interrupted or with a continuous suture of silk or Supramid Extra (R) (5-0). We prefer the latter because of its great strength and total lack of tissue reaction.

The causes of intractable blepharospasm in our third and fourth patients were the excessive blinking with keratitis sicca in highly nervous patients. Though our fifth patient had many neuroses and was under psychiatric care, the technique as described has decreased the 'clenching' effect of the orbicularis.

## DISCUSSION

Many questions were raised by members of the Congress as to the cause of intractable blepharospasm and whether there was danger of a complete paralysis of the orbicularis. The causes of this condition are usually photophobia from various diseases, keratitis sicca, and other conditions that cause frequent blinking; all of the patients that I have seen were high strung nervous personalities. Orbicularis paralysis has never occurred in our series.

Dr. Lester T. Jones, of Portland, Oregon, kindly read over this article and has suggested a possible improvement of the method to control intractable blepharospasm. He does not resect the muscle, but destroys the nerve supply. He injects the local anaesthetic starting at a point approximately 25 mm. lateral to the lateral commissure and infiltrates the subcutaneous area above and below this point. An effort should be made not to get the anaesthetic into the submuscular space. A vertical incision is made through the skin and superficial fascia down to the muscle, extending above and below the point of injection. The incision should curve slightly medially above and below and have a total length of 3 or 4 cm. The muscle fibers are separated just enough to expose the submuscular fascia in which the facial nerve fibers are located. The central 2 cm. of this fascia is cut through, exposing the bone and deep muscle fascia. This should weaken the lateral half of the palpebral muscles. If more weakening is necessary, the patient may be asked to squeeze the eye shut or a square wave or Faradic type bipolar stimulator may be applied to determine how far above and below the nerve fibers should be cut. The nerve fibers that cause contraction of the medial  $\frac{1}{2}$  to  $\frac{1}{3}$  of the palpebral muscles should be avoided. It may be possible in the upper part to bypass these fibers and then cut enough of the fibers going to the corrugator to weaken its action.

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FIG 1 (Callahan) A curvilinear incision is made through the skin and subcutaneous tissues the postero-lateral edge of the orbicularis muscle is exposed and a sector about 10 mm wide and 40 to 50 mm vertically is resected. The sub-muscular fascia is not incised because the motor nerve supply lies between the muscle and the submuscular fascia. Sometimes the nerve supply to the corrugator must be resected but the nerve supply of the frontalis should not be

FIG 2 (Callahan) A highly nervous patient had extreme photophobia from slowly developing cataracts and developed intractable blepharospasm. To see he had to hold his lids and eyebrows up with his fingers.



FIG 3 (Callahan) Six months after most of the nerve supply to the orbicularis was removed. In none of our patients has too much orbicularis been resected for the patients have had no difficulty in closing their eye lids.

It is unnecessary to remove tissue posterior to the orbicularis muscle and there is no danger of causing a facial paralysis if one does not extend the section further back than the orbicularis. It is always surprising to see how much orbicularis contracture can still occur when a large part of the nerve supply has been disconnected.

After the orbicularis resection, the subcutaneous tissues are drawn together over the defect and united with interrupted gut sutures (1-0).

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FIG 1

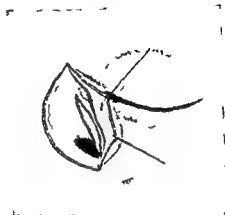


FIG 2

the periosteum in front of the anterior lacrimal crest the periosteum is widely separated from the bone to enable the tissues to be retracted by a few deep traction sutures. The lacrimal sac enclosed in periosteum is mobilised laterally from the lacrimal fossa (Fig 2)

Every operation has its signposts and its rallying point. Just as the anterior crest is the signpost for the lacrimal sac, so the medial palpebral ligament is the signpost for the common canaliculus and a traction suture through its detached medial end is of great value whilst the dissection is deepened between the sac and the ligament by means of Rollet's rugine (Fig 3). As we have seen, this brings us directly down on to the common canaliculus with the least disturbance of the insertions of the important portions of the orbicularis on to the lateral surface of the posterior part of the palpebral ligament. Care is needed because we are working through tough fibrous tissue down on to



FIG 3

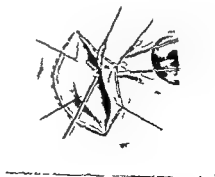


FIG 4

# CANALICULODACRYOCYSTORHINOSTOMY

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Obstruction in the lacrimal canaliculi near the sac is fairly common, in London it probably accounts for 10% of epiphora requiring surgery (Jones, 1960). The literature records many attempts (Rycroft, 1960) but reveals no method of curing the condition with a degree of certainty approaching that given by the technique which I here present.

## AETIOLOGY OF OBSTRUCTION OF THE COMMON CANALICULUS

The two canaliculi often join together at their medial ends to form a short common canaliculus. This passes medially through the posterior portion of the medial palpebral ligament and lacrimal fascia (Jones, 1957) to reach the lacrimal sac. The appearance, relations and surgical behaviour of this little tube is seen in 10 operations upon it, leave no doubt that it is better described as a common canaliculus than as a sinus of the sac.

In *primary stenosis*, which accounts for 32 of my 40 cases, the common canaliculus is squeezed by this tight fibrous tissue through which it passes to join the sac (Jones, 1960).

Acute, or occasionally chronic, dacryocystitis may lead to a *mucosal occlusion at the entrance of the common canaliculus into the sac*, as in 8 of my 10 cases.

*Mucosal obstruction* of the common canaliculus was caused by irritation in 2, erythema multiforme in 1, trachoma in 1 and conjunctivitis of unknown aetiology in another case.

*Traumatic avulsion* of the common canaliculus also occurs at this site.

## THE TECHNIQUE OF CANALICULODACRYOCYSTORHINOSTOMY

My operation consists essentially of dissecting out the common canaliculus and a little of both upper and lower canaliculi removing any strangling fibrosis in the region of the medial palpebral ligament anastomosing the common canaliculus with the sac and completing the procedure with a dacryocystorhinostomy.

The usual approach to the lacrimal sac is made through a straight incision well forward on the side of the nose (Fig. 1). Bleeding points are picked up in non-toothed dissecting forceps and rapidly coagulated by diathermy applied to the forceps. The incision is deepened through

submucous resection of a portion of the middle turbinate, should it interfere large flaps of nasal mucosa can always be fashioned so that they will enable the sac to swing out laterally to make good the shortening resulting from the anastomosis of canaliculi to sac

Having cleared up any stray fragments of bone the sac is incised from end to end along its medial aspect (Fig 6) It is then swung medially and the common canaliculus is snipped off as close to the sac as possible If the obstruction extends far laterally it is necessary to incise down on to the probes but in any event the common canaliculus is slit along its upper and lower borders to form an anterior and a posterior flap Four Kalt silk sutures are passed on Jameson Evans or Grieshaber 82-5 needles one through each corner of the flaps of canaliculus These are passed through a short incision in the lateral wall of the sac the flaps of common canaliculus are pulled through on to the inside laid back and sutured to the mucosal surface of the sac (Fig 7) It is essential to completely mobilise the common canaliculus and sufficient of its tributaries to enable these flaps to be brought cleanly through inside the sac Often a few extra sutures are required to splay out the common canaliculus

In order to keep this anastomosis of canaliculus to sac cleanly open and lightly on the stretch with no possibility of it touching any other tissue I always combine it with a rhinostomy (Fig 8) Careful suturing of posterior and anterior flaps of the rhinostomy keeps the sac on the stretch from front to back and this is made more certain by hitching the sutures in the anterior flap forwards to the periosteum (Figs 9 & 10) Nothing is to be gained by leaving large catheters lying around in such a rhinostomy but it is my custom to pass one end of a fine polythene tube from the upper punctum through the anastomosis of canaliculus to sac and out through the nose and then to pass the other end similarly through the lower punctum This tube serves

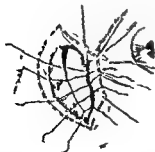


FIG 9

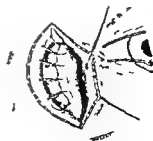


FIG 10

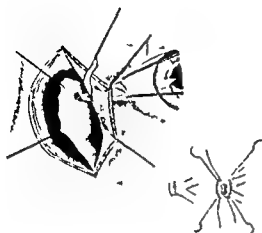


FIG 5

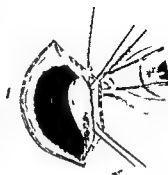


FIG 6

delicate tubes whose position is defined by having a probe in each canaliculus. The mobilization of the common canaliculus is the rallying point of the operation but it is essential to separate this tube from the remaining portion of the ligament passing behind it to the posterior lacrimal crest (Fig 4).

At this stage I swing the sac laterally and proceed to remove the bone for the rhinostomy. I remove a large area of bone extending forwards from the posterior crest to a point in front of the anterior crest and from about five millimetres above the fundus of the sac right down to include the party wall between nasolacrimal duct and nose (Fig 5). It happens to be my preference to use the Fraquair separator followed by bone punches and nibblers and for some portions the gouge, because, in my hands at least, these are the most versatile tools. By excising any obstructing ethmoid cell and carrying out

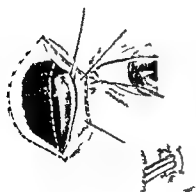


FIG 7



FIG 8

avoided. This technique is applicable if the obstruction extends along one or both of the canaliculi. For in this instance it is possible to anastomose either the upper or the lower canaliculus to the sac by splitting the little tube into an anterior and posterior flap (Fig. 11). It is worth



Fig. 11

attempting if half of the lower canaliculus is patent. Five out of six such cases have been entirely successful and it is especially gratifying to have cured two patients with the difficult post irradiational obstruction.

### SUMMARY

Obstruction in the common canaliculus near the sac accounts for about 10% of epiphora. All but one of 40 cases have been cured by dissecting out these passages, splitting the common canaliculus to form anterior and posterior flaps, pulling these through an opening into the sac and suturing them apart inside the sac. Careful suturing of the sac to the nasal mucosa completes the canaliculodacryocystorhinostomy.

### RESUME

L'obstruction du canalicule commun pres du sac lacrymal est responsable d'environ 10% des cas d'epiphora. A part une seule exception, 40 malades ont ete gueries par la dissection des voies lacrymales, la division du canalicule en deux lambeaux, l'un anterieur, l'autre posterieur, que l'on tire par une breche pratquee dans le sac et la suture des lambeaux separement a l'interieur du sac. La canaliculodacryocystorhinostomie est completee en suturant avec soin le sac et la muqueuse nasale.

### ACKNOWLEDGEMENTS

In presenting this procedure I am indebted to Professor Rowland Wilson, University of Otago, N.Z., who first confronted me with the

merely as a splint whilst the surfaces are healing and I remove it after a week or two. In closing the wound, it is important not to attempt to suture the palpebral ligament to the periosteum because, having divided its deep attachment to the posterior lacrimal crest, the resulting pull forward and usually may displace the puncta away from the globe.

It is clear that what matters to the patient is what is done to him rather than what tools are used, but these two double dissectors, one being sharp and modelled after a Tooke's knife, straight and angled, and the other having a sharp rugine at one end and a semi-sharp spoon at the other end, facilitate the dissection. The suturing of these fine flaps of mucosa within a rather awkward and restricted field is considerably facilitated by a pair of angled crocodile needle holding forceps which Meyer and Phelps have made to my specification. The needle can be held at any angle, the smooth surfaces are a delight in tying the knots and the unobstructed view it allows is a great advantage.

#### POSTOPERATIVE MANAGEMENT

Until the polythene tube is removed after a week or two, Albucid drops keep the eye clean. It is important to relieve postoperative nasal congestion and remove mucus and blood clot with *Narist* ephedrine 1% in normal saline twice daily until the nasal surfaces have healed cleanly. The sutures in the anastomoses usually fall out within the first few months — if not I remove them through the nose.

It is important to watch some cases carefully during the first three months. Of 10 operations, 6 have shown a tendency to closure at the site of the anastomosis of canaliculus to sac. With the gentle passage of probes this tendency was overcome in all but 2. After the third or fourth month the condition has remained stabilised.

The only other point requiring attention has been a slight eversion of the lower punctum in half the cases during the first month. This may be very easily overlooked unless the lid margin is examined from above with the patient looking up. In 5 cases the crutery was required to correct the position of the punctum.

#### DISCUSSION OF RESULTS

Thirty eight of the 10 operations have given completely dry eyes. It is possible to repeat the canaliculus to sac anastomosis and in this way I have cured one of my failed cases, the other is waiting admission for this.

The operation has been in use for 7 years and no case which was initially successful has shown any tendency for late closure. I believe that the two crucial points in the success of this procedure are the two points in which it differs fundamentally from alternative methods: firstly the fibrous tissue that is strangling the canaliculus is dissected away, secondly by bringing the canaliculus into the sac and splinting its ends apart anything approaching an end to end anastomosis is



## NEW TREATMENT OF PTERYGIUM

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The pterygium is possibly produced from the pinguecula which has degeneration of conjunctival connective tissue due to acquired stimulation from outside. On this point, some investigators have the same opinion. However the reason why the degeneration of connective tissue extends to the corneal connective tissue is unknown.

The authors have an opinion that the focus of the pterygium is present in the head which has intensely degenerated mass of connective tissue as the pattern of figure 1. From the focus the degeneration advances further to the centre of the cornea. In this process it passes between the corneal epithelium and the Bowman's membrane, and



FIG 1

produces swelling or thinning or irregular curvature on the latter. At last Bowman's membrane is destroyed and parenchymal fibres directly under the membrane show degeneration. On the other hand, in regard to the limbal side the degenerated mass of connective tissue of the head has firm tendency to be repaired gradually by regenerated fibres due to propagated fibroblasts and invaded blood vessels. On more close area to the limbus the corneal tissue regains completely its normal thickness and curvature although the Bowman's membrane is absent in the area. However the degenerated mass which is pushed out of the cornea is replaced by the conjunctival connective tissue.

condition, to the Surgeons of Moorfields and the London Hospital who encouraged me to carry out this operation, to Miss M. George for her help with the radiology and to Mr T. R. Tarrant and to our Department of Medical Illustration who prepared the illustrations.

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removed. No suture is placed. In the procedure, attention must be placed on the following points:

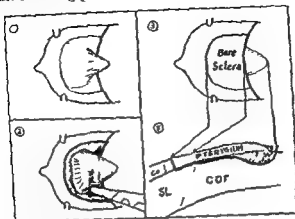


FIG 2

- To remove completely the head of the pterygium which has the degenerated tissue
- To expose the sclera completely by thorough stripping and the removal of the body of the pterygium with Tenon's capsule from the sclera
- Degenerated mass in the cornea must be removed completely. At this time, one must avoid excessive removal of normal corneal tissue. Especially, on the limbus the removal is limited to the superficial layer as figure 2(3) in order to expect easy repair.
- Normal conjunctiva which connects with the upper and lower borders of the pterygium must be removed. Fluck line on figure 2(1) shows the line of the removal. When the defect of conjunctiva is too wide to be repaired, the line of removal must be put along the dotted line.

The area of the wound due to the above procedure consists of the following parts. They are the conjunctival area and the corneal area. In regard to the former the conjunctiva is removed and the sclera is exposed on the area which spreads from the muscle terminal to the limbus. In regard to the latter the lamellar defect which reaches the corneal parenchyma is formed.

### 3. RESULTS OF THE OPERATION

On the next day of the operation on all cases the bare sclera is clear and dilated capillaries run on it. Notable signs of inflammation are not observed. The course which received two TEPA instillation was as follows.

After 3-4 days from the beginning of instillation, the surface of the wound is covered by fibrin mass (Fig 3). Afterwards with the lapse of days fibrin mass decreases and vascularization invades from

with blood vessels. On the occasion, the latter becomes the same figure as that of the normal conjunctival tissue. Afterwards, it occasionally takes on a cicatrice like feature by the occurrence of partial fibrosis.

## 1 NEW TREATMENT OF THE PTERYGIUM

During the operation, it is advisable to remove the degenerated mass of the head, completely, because the source of the pterygium is the degenerated mass of connective tissue in the head.

The procedure is important to prevent the recurrence. In regard to the neck, the same care is needed, because a part of the degenerated mass is present in the corner. On more adjacent part to the limbus, where normal thickness and curvature of the normal corneal tissue are regained, degenerated mass is present in the conjunctival like tissue which rides on the corner. Therefore, a single removal of conjunctival like tissue is satisfactory.

However, even when degenerated focuses are removed completely, the recurrence occurs when operative defect of the tissue is replaced by conjunctival granulation. The most important procedure to prevent the recurrence is to inhibit the granulation which is produced on the wound of the conjunctiva. Moreover, it is necessary to prevent the invasion of granulation into the operative defect of the corner. Recently irradiation with use of  $Sr^{90}$  has been performed. This method is inadequate to meet the above condition. When granulation does not invade the corneal defect, a natural regeneration of the corner begins. This process is slow, however, the defect is repaired. Invasion of vascularization is not observed, on the occasion.

To satisfy the above condition, the authors used thio TEP-1 and mitomycin C which are so called oncostatic preparations. These preparations have the power to suppress the formation of granulation on the corner and conjunctiva, and the effects are not inferior to  $Sr^{90}$ .

1 mg/ml thio TEP-1 diluted by physiological saline and 0.1 mg/ml mitomycin C diluted by 5% glucose were prepared. Instillation of these solutions were performed 3 times a day during 1-2 weeks after the operation. The procedure of the operation is as follows.

## 2 THE TECHNIQUE OF THE OPERATION

The authors performed bare sclera method. As figure 2, 4-6 mm from the limbus, an incision is placed on the body of the pterygium along the limbus. The incision is elongated and the body of the pterygium is cut. Normal conjunctiva is exposed. Horizontal incision is placed on the normal conjunctiva up to the limbus. Lobe like body of the pterygium is striped from the sclera completely, with Tenon's capsule. When the striping reaches to the limbus, a small piece of a razor which is snapped off to adequate size is picked up with a razor blade fragment holder as a sickle. The blade of the razor is inserted under the lobe like tissue and advanced in the corner from the limbus to the apex of the pterygium, as figure 2(2). Finally, the pterygium is

due to an allergic reaction involving a wide variety of antigens. The vessels may become sensitized through an intraocular antigenic source (lens protein, uveitis) or from an extraocular source (pulmonary tuberculosis, brucellosis), or possibly from the formation of complex autoantibodies in multiple sclerosis.

Eales's disease is one clinical form of retinal vasculitis, usually of unknown aetiology and characterised by recurrent peripheral haemorrhages in young males. The two terms of Eales's disease and retinal vasculitis should not be used synonymously. Regarded in this way it is not surprising that Eales's disease may have multiple causes or that it should sometimes present with vasculitis elsewhere in the retina or nervous system or with other allergic manifestations in the uvea or in the body generally.

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However when the tendency to form granulation is vigorous, granuloma is formed (Fig 5) and occasionally, then develops into a recurrence of the pterygium

Secondly the course of mitomycin C instilled cases is related During the interval from the 1st day to the 5th day permeation occurs on the surface of the wound and the surface becomes covered by fibrin mass Afterwards, the fibrin mass rapidly disappears Permeation is more slight compared with tho TEPA instilled cases But the tendency to form granulation is weak The surface of the wound takes the appearance of a normal conjunctiva after 20-40 days

The results of the operation on which tho TEPA or mitomycin C instillation was combined were illustrated on Table 1

Table 1

After Operation (Months)	Tho TEPA		Mitomycin C	
	Total	Recur	Total	Recur
1 — 3	5	0	10	0
4 — 6	8	2	7	0
7 — 12	10	2	—	—
13 or more	8	1	—	—
TOTAL	31 (83.9%)	5 (16.1%)	17	0

Table 2

Days	AEEP 17.25 C — 30 C		
	Purity (%)	pH	Appearance
0	100.00	7.1	Uncolor almost transparent
10	98.81	8.65	
16	97.36	—	
21	93.65	8.65	Polymeric Compound partly precipitate
30	87.83	8.55	Polymeric Compound precipitate
60	66.89	8.5	
90	50.20	8.5	

Stability of aqueous solution of Tho-TEPA

the adjacent conjunctiva and the surface of the sclera. Then, a partial granulation is formed.



FIG. 3



FIG. 4



FIG. 5

Afterwards, this process proceeds gradually and the surface of the wound is repaired from the periphery. After a certain period, the granulation disappears gradually and the surface shows the same appearance as that of the normal conjunctiva (Fig. 5). It takes 1-2 months to reach this state.

■ performed again and continued for a week. For few obstinate cases instillation and  $\text{Sr}^{90}$  irradiation was combined.

Instillation of thio TEPA or mitomycin C had no significant side effect. However, the former provoked allergic conjunctivitis on 2 cases.

## CONCLUSION

The authors investigated the genuine nature of the pterygium by biomicroscopical and histological studies and found a new treatment. The degenerated foci in the cornea, and the body and neck of the pterygium, were removed. Bare surface of the wound was not covered. Postoperative instillation of oncostatic preparations (Thio TEPA and Mitomycin C) gave favourable effects which were no inferior than the effect of  $\text{Sr}^{90}$  irradiation. This method was very effective for the operation of recurrent pterygium and for aid in other conjunctival operations.

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5. Thio-TEPA = Tepamun (Sumitomo Chemical Co. Ltd Higashi ku Kitahama 5-22 Osaka Japan).
6. N. N. Triethylen Thiophosphoramide  
 Color of Crystal Colorless crystal or white crystalline powder  
 Molecular weight 189.27  
 Tentative molecular form  $\text{C}_3\text{H}_{12}\text{N}_3\text{P}_3\text{S}_3$   
 Melting point 52-53°C.  
 Easily soluble in Alcohol Ether Benzene Acetone Etheracetate  
 Sparingly soluble Petroleum ether  
 pH 6.5 (Aqueous solution 1:10)  
 Mitomycin C (Kyowa Hakko Kogyo Co. Ltd Tiyoda ku Otomachi, 1-4 Otomachi Building Tokyo Japan)  
 Streptomycin caespitosus ~ 1956 T. Hata ~ Fraction V  
 Color of Crystal Deep bluish violet.  
 Elemental Analysis C = 53.11 H = 5.14 N = 15.49  
 Molecular weight About 1120 (When m-dinitrobenzene was used as solvent ~ Rast method ~)  
 Tentative molecular form  $\text{C}_{42}\text{H}_{54}\text{N}_{10}\text{O}_{16}$  (Calculated C = 54.22 H = 5.14 N = 15.22 O = 23.42)



Table 3

	pH	0	1	2	10	20 Days
5°C	7.0 8.0	100 100	100 88.9	98.5 99.0	82.6 82.2	56° 88°
27°C	7.0 8.0	100 100	90.6 88.6	— —	71.5 78.7	— —
37°C	7.0 8.0	100 100	88.0 91.8	87.1 94.5	35.6 84.5	— —

Stability of aqueous solution of mitomycin C at each temperature at pH 7.0 and 8.0

## DISCUSSION

The unique points of the authors' operation are to expose the sclera widely and to leave bare part without any cover or implanted graft. Generally, such procedure forms hard granulation on the surface and the granulation rapidly covers the surface, then, invades in the corner. Conjunctival granulation makes cicatrice and contraction in the future. Indeed, the pterygium is produced again and the disturbance of ocular movement or convergent strabismus is provoked. When oncostatic preparations are instilled, the formation of granulation is suppressed. In the majority, the granulation is not formed. Even when small granulation is formed, it disappears naturally. Normal conjunctiva regenerates on the surface of the wound and the pterygium completely heals.

On the occasion, the defect of the cornea and the conjunctiva gradually receives natural repair from their respective connective tissue cells and epithelial cells. Vascularization into regenerated conjunctiva is very slow.

When this TTPA and mitomycin C are compared to each other, the former gives more intense stimulation on the surface of the wound than the latter. Consequently, the authors reached a conclusion that instillation of mitomycin was superior.

However, even when the pterygium was treated by the authors' new method, the zero rate of recurrence was not attained. 2-4 weeks after the operation, the state of limbus and the adjacent part was investigated in detail. When the blood vessels show the tendency to invade the cornea, it is necessary to remove a small part adjacent to the limbus and to instill this TEP or mitomycin C after the removal for a week.

In regard to the operation of the recurrent pterygium or the cases of post-operative hard granulation, instillation after the operation is continued for a long while, or after a certain period, the instillation

## Case 1

5 years old male (Fig 1) had right gradual proptosis of six months duration. Proptosis increased on weeping. The right eye showed a downward and inward severe proptosis of 30 mm. Hertel (Left eye 15 mm) with limitation of ocular movements in all directions. There were oedema of lids and chemosis of the conjunctiva. A tense cyst was felt in the upper outer part of the orbit. The cornea showed a corneal ulcer — due to lagophthalmos — preventing a clear view of the fundus. Vision was 1/60.

Under general anaesthesia and through a skin incision performed along the upper outer orbital margin a large, transparent tense cyst related to the orbital lobe of lacrimal gland, was seen extending backwards into the orbit. The cyst ruptured during its blunt little finger dissection and about 15 cc clear watery fluid came out. This was followed by spontaneous sliding of a mucoid cyst out of the wound. Immediately the proptosis, oedema of lids, and chemosis of the conjunctiva disappeared. The orbital part of the lacrimal gland was found firm lobulated greyish in colour. A biopsy of the gland was taken.

The mucoid cyst (Fig 2) was translucent  $3 \times 4$  cm in size with a smooth surface and containing clear fluid. On histopathological examination the cyst proved to consist of mucoid material. The lacrimal gland tissue showed a mild chronic non specific interstitial inflammation (Fig 3).

(Fig 4) shows the child two weeks after the operation.

## Case 2

25 years old woman (Fig 5) complained of a painless gradually developing swelling of her right upper lid of seven months duration. The right upper eyelid showed ptosis. On elevating the upper lid a large tense smooth, transparent  $3 \times 2$  cm cystic swelling which could be transilluminated was found projecting into the upper conjunctival cul de sac (Fig 6). The right eye was normal fundus normal vision 6/9.

After an upper fornix conjunctival incision the cyst was easily separated from the surrounding tissues. Histopathologically the cyst proved to consist of mucoid material being a mucoid cyst of Krause's gland duct. Biopsy of the fornix subepithelial tissues surrounding the cyst showed a chronic non specific interstitial inflammation of Krause's glands. (Fig 7) shows the patient one week after the cyst excision.

In both cases the cyst was full of clear colourless thin watery fluid similar to tears. The fluid was alkaline in reaction. Cultures proved absence of organisms. On microscopic examination the fluid contained only few degenerated epithelial cells. The biochemical analysis of the fluid showed the presence of protein material sodium chloride urea sugar phosphates in the same percentage as in tears.

Follow up of the two cases for two years showed absence of cyst recurrence.

## MUCOID CYSTS OF ORBITAL LOBE OF LACRIMAL GLAND AND OF KRAUSE'S GLAND

### Report of Two Cases

AIY MORTADA, M S \*

Cysts of the lacrimal gland are classified as retention cysts of the palpebral lobe "Dacryops", cysts of the orbital lobe, hydatid cysts and dermoid cysts. Although dacryops are relatively of frequent occurrence, cysts of the orbital lobe and cysts of Krause's glands especially cysts of mucoid nature were rarely reported in the literature.

Most cystic formations occurring in the orbital lobe are congenital in nature or neoplastic in origin (Duke Elder 1952). Retention cysts of the orbital lobe were recorded by McMullen (1920) and Vrabec (1918). Congenital cysts of the orbital lobe may appear clinically immediately on birth or be delayed for some years (Van Duyse and Van Iant 1922, Wood 1930 and others). Schornstein (1936) described such a congenital cyst showing highly vascularized tissue wall rich in capillary network and multilayered epithelium.

Cysts of Krause's glands are rare and usually occur as retention cysts in cicatricial conditions of the conjunctiva such as trachoma, or pemphigus (Stower 1892, Thompson and Chatterton 1905, Contino 1906, Crocci 1932 and others) or after scar caused by excision of chalazion (Paton 1919). Giri (1936) and Butler (1907) reported cases where in no conjunctival scarring was evident.

### Case Reports

In the two cases of mucoid lacrimal glands cysts to be described the general condition of the patients was good. Family history was of no importance. There was no history of trauma. There was no septic foci in the body or any genito urinary gonorrhoeal infection. Blood total and differential counts were normal. Blood Wassermann reaction, Casoni's test for hydatid cysts and tuberculin test were negative. Faeces were free of parasites and urine was free of albumin and sugar. X ray of both orbits, nasal sinuses and chest revealed normal findings. The left eye in both cases was normal with normal fundus and vision 6/9.

Right and left eyes in both cases showed palpebral and fornix conjunctival trachomatous scarring. Conjunctival smears and cultures were negative for organisms. There was no chronic dacryocystitis.

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CASE 2

FIG 11 Mucoid cyst of right upper Krause's glands in a woman aged 25 years  
Note swelling of upper lid and ptosis



FIG 6 Translucent large mucoid cyst of Krause's glands. Upper lid is elevated to expose the cyst



FIG 7 Patient two weeks after removal of mucoid cyst of Krause's glands

# DISCUSSION

In dacryops the lining of the cyst may resemble that of the ductule being composed of double layer of epithelium (Wiedersheim 1928 and others) in others there is a single layer of cylindrical epithelium (Gorlitz 1917 and others) in others the second layer is flattened endotheloid like cells (Goldzieher 1905 and others) or in others again goblet mucous cells are evident (Toth 1944 and others), while occasionally there are several layers of cells or profuse epithelial proliferation (Weckers 1909 and others). Probably many of these cysts were conjunctival cysts present in the upper outer conjunctival fornix as in many of them goblet cells were present among the cyst epithelial lining and in others several layers of epithelium were present.

In the two described cases the presence of conjunctival trachomatous scars throws a light on the cause of the low grade chronic interstitial inflammation of the lacrimal gland or Krause's glands and the

## CASE 1

FIG 1 Mucoid cyst of orbital lobe of right lacrimal gland in a male child aged six years. Note severe proptosis.



FIG 2 To the left is the large translucent mucoid cyst of orbital lobe of lacrimal gland. To the right a piece of lacrimal gland removed for biopsy. Note graduations in inches.

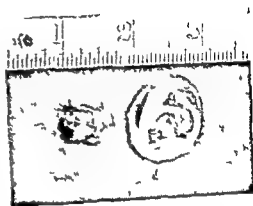


FIG 3 Orbital lobe of lacrimal gland showing chronic non-specific interstitial inflammation ( $\times 540$ ).

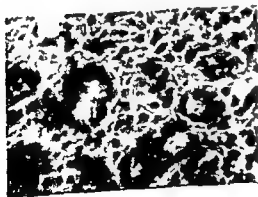


FIG 4 The child two weeks after excision of the mucoid cyst of the orbital lobe of lacrimal gland. Notice absence of proptosis.



## AMYLOIDOSIS OF THE CONJUNCTIVA WITH REVIEW OF 21 CASES

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Amyloid disease of the conjunctiva and eyelid is a rare but well authenticated entity. It was first described by Von Oettingen (1871) and then investigated in Russia by Raehlmann (1881), Kubli (1881) and Vossius (1889). Reports in the English literature are few in number. Brief mention of the disease has been made by Fuchs (1919), de Schweinitz (1921), Collins and Mayo (1925), Wolff (1934), Berens (1936), Duke Elder (1938), Wiener (1946) and Castroviejo (1946). Ellis (1915) reported amyloid disease of the conjunctiva in a 30 year old woman who had mild conjunctivitis of the right eye for 2 years and hard induration of the lower lid for 34 months. Guerri and Wiesinger (1960) have reported a case of primary amyloidosis of the eyelids and conjunctiva in a woman of 62 years of unknown aetiology.

Amongst Indian observers cases have been reported by Reddi (1948), Srinavasan (1949), Wahi and Wahi (1954), Srivastava and Agrawal (1958), Mathur and Mathur (1959) and Ishwar Chandra and Sharma (1960) and recently by Darbari and Sehgal (1962).

### CLASSIFICATION AND AETIOLOGY

Primary systemic amyloidosis is a rare disease of unknown cause. Out of all the cases reported, very few showed an involvement of the conjunctiva. Reimann et al (1935) have recognised four varieties of amyloidosis: (1) Primary, (2) Secondary, (3) Localised amyloid tumour and (4) Amyloidosis associated with multiple myelomata. Of these secondary amyloidosis is the most common form and is associated with long continued infective tissue destructive processes such as tuberculosis, leprosy and osteomyelitis etc. The organs most often involved are spleen, kidneys, liver and adrenals. Primary amyloidosis, which occurs in the absence of any known predisposing disease, tends to involve the mesodermal tissues such as smooth and skeletal muscles, cardiovascular system and skin.

Most authorities have now accepted the contention that primary and secondary amyloidosis are closely related. No clear cut distinction can be made between the two on the grounds of (1) Morphology of deposits including the staining characters, (2) Distribution of deposits, (3) Pathogenesis and (4) Chemistry. According to Symmers (1956)

cause of mucoid degeneration of affected lacrimal or Krause's glands duct epithelial lining. Also the trichomatous conjunctival scars are the cause of obstruction of the degenerated duct which distends by retention of tears giving the described clinical picture of mucoid cyst of orbital lobe of lacrimal gland or of Krause's glands.

The three theories put for the formation of lacrimal gland cysts explain the formation of such mucoid cysts: the presence of mild chronic inflammatory process around the ductules (Sourdille 1899), the presence of mucoid degeneration of duct epithelium (Goldzieher 1905) and the obstruction and dilatation of the excretory duct blocked by inflammatory influences (Lange 1899).

### SUMMARY

1 Mucoid cysts of orbital lobe of lacrimal gland and of Krause's glands were rarely recorded in the literature. The two reported cases represent the largest cyst of this kind and the first to be described from Egypt.

2 In the two described cases mucoid degeneration of the affected lacrimal ductule was due to chronic dacryodermatitis probably of trichomatous origin. Obstruction and thus distension of the mucoid cyst with tears were due to trichomatous conjunctival scarring.

3 Mucoid cysts of the lacrimal gland or Krause's glands are loosely attached to their surrounding tissues and are thus easily removed.

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XIX CONCILIUM OPHTHALMOLOGICUM

1962

INDIA  
(NEW DELHI)

ACTA

VOL II





# EXPERIMENTAL ASPECTS OF EALES'S DISEASE

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In spite of the fact that 80 years have passed since the first description of Eales's disease by Henry Eales the etiology, methods of treatment and prophylaxis related to it have not yet sufficiently elucidated. It is not even certain as to what the complete definition of this disease is. Consequently it may be supposed that etiology of this disease is not easily defined by the experimental methods heretofore studied using of clinical cases.

## CLINICAL ASPECTS

In the present studies statistical analysis were carried out in 133 cases of recurrent intraocular hemorrhage in which definitely diagnosed systematic diseases were not included. The age of the patients was generally young covering from 15 to 58 but most fell in the younger category of 15 to 35 (Table 1). Out of 133 cases 103 were male and 30 female. The right eye was affected in 51, left eye in 46 and both in 36 eyes.

The important diseases in the patients past histories include lung tuberculosis, rheumatism, constipation, epistaxis, icterus, kidney disease, gastroptosis, anal fistula, hookworm disease, anaemia, tonsillitis and so on. As eye complications, uveitis, iridocyclitis, cataract and glaucoma were observed. The skin tuberculin test was positive in 40 and negative in 9 of the 51 patients which showed accurate clinical history in the card and 21 patients out of 133 had long tuberculosis in their past histories (Table 2).

Besides these 133 patients the author observed a few cases who had clinical entity like Eales's disease and had both primary retinal and retino vitreous hemorrhage in old age. That is uncertain whether or not these cases should be classified as Eales's disease or whether there must be further elucidation.

Also from the standpoint of classification it may be supposed that some cases might develop from different cause e.g. previous case, Buerger's disease, sepsis and anaemia even though tuberculous symptoms existed were proved in the greater number of cases. Consequently in the studies of Eales's disease a more thorough examination of the etiology is first problem to be solved and clinical explanation especially problems of the treatment may be of secondary consideration.

of hypertrophy of the tarsal plate and the conjunctiva were subjected to histopathological examination the number of such cases would be much greater. Our 21 cases can be reviewed as follows —

Male = 15 cases

Female = 6 „

#### Age Incidence

10-20 years = 5 cases

21-30 „ = 10 „

31-40 „ = 4 „

Over 41 „ = 2 „

It is obvious that it is more common in males and in the age period between 21-30 years. On the other hand trachoma is more active in the younger age period i.e. between 1 and 10 years. One may conclude that it is not the activity but rather the chronicity and repeated irritation that predispose the lids to such amyloid deposits and tumour formation. One of these cases had chronic dacryocystitis as well and it was this eye which developed amyloidosis. Like pterygia it is more common in males as they are constantly exposed to repeated irritations.

Unilateral = 15 cases

Both lids = 8

One lid = 8

Bulbar conjunctiva also affected = 6 cases

In one case all the four eyelids were affected

#### CLINICAL APPEARANCE

The patients were quite healthy unlike cases of amyloid disease of kidneys or intestines. The upper lid was affected more commonly (Fig. 1) leading to tumour formation with mechanical ptosis and



FIG. 1 Amyloidosis affecting the upper lid

the only criterion for primary amyloidosis is the absence of a recognised predisposing cause

Localised amyloidosis forming a small tumour like growth has been described in many sites including the respiratory tract, tongue, pharynx, thyroid, etc., but the aetiology of such amyloid deposits in the ocular tissues particularly in the lids is obscure Reddi (1948) Srinivasan (1949), Mathur and Mathur (1959), Ishwar Chandra and Sharma (1960) all think that it is secondary to trachoma or some other chronic irritation like dacryocystitis or chronic conjunctivitis Wahu and Wahu (1954) could not suggest an aetiological agent in their own case Ellis (1915) in her report suggested nutritional deficiency as a possible aetiological factor and Ashton described amyloid degeneration as a subgroup of hyaline infiltration of the eyelids In this respect he agreed with Duke Elder and Schmiedeberg (1920) who consider hyaline as a transitional product in the formation of amyloid from albumin Boyd (1960) thinks that all varieties of amyloidosis are probably related to one fundamental disturbance, the nature of which is still obscure It is also surmised that it may be a manifestation of hypersensitivity in which antibody is precipitated with polysaccharides of the ground substance Similarly Gilkes suggests that hyaline and amyloid degeneration of the conjunctiva may be regarded as variations of a single process where hyaline material is formed in the tissues as the result of a perversion of local protein metabolism Its extent to which this takes place will govern whether the appearances formed be those of hyaline or amyloid material

The aetiology of the disease is obscure in some cases as it is seen in normal individuals and clinically healthy eyes while in others it is secondary to some chronic irritative focus As the incidence of amyloidosis is greater in countries where trachoma is highly prevalent and that part of the conjunctiva most affected by the trachoma virus is more frequently involved, it appears that it bears a definite relationship to trachoma particularly in cases with a prolonged second stage Pathological examination of our cases also suggests this fact It also appears that conjunctival amyloidosis may not be so infrequent as is suggested in the literature

#### REVIEW OF 21 CASES

We have come across in our records of the past 71 years, 21 cases which were admitted, investigated and operated upon in our hospital This is actually an underestimation of its incidence as some of the cases refused operation while in others the diagnosis was so obvious that the tissues were not sent for histological examination Three cases diagnosed by the pathologist as phlyctenulosis are not included though they can also be grouped because they also stained metachromatically with methyl violet The incidence of trachoma in northern part of India varies from 54 per cent in the plains to over 80 per cent of population in the hill areas It is, therefore to be expected that amyloidosis would be more prevalent here We also feel sure that if all the cases

of hypertrophy of the tarsal plate and the conjunctiva were subjected to histopathological examination the number of such cases would be much greater. Our 21 cases can be reviewed as follows —

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#### REVIEW OF 21 CASES

We have come across in our records of the past 7½ years, 21 cases which were admitted, investigated and operated upon in our hospital. This is actually an underestimation of its incidence as some of the cases refused operation while in others the diagnosis was so obvious that the tissues were not sent for histological examination. Three cases diagnosed by the pathologist as plasmocytoma are not included though they can also be grouped because they also stained metachromatically with methyl violet. The incidence of trachoma in northern part of India varies from 54 per cent in the plains to over 80 per cent of population in the hill areas. It is, therefore, to be expected that amyloidosis would be more prevalent here. We also feel sure that if all the cases

One of our cases was especially interesting since he gave a history of recurrent conjunctivitis the last attack lasting for nearly six months and he showed a papillary hypertrophic form of trachoma, stage II (M Callan's). The conjunctiva usually presents a half cooked potato appearance. This appearance can be well appreciated during operation.



FIG 5 (M. P.) Amyloidosis with calcification. The section shows fibrocollagenous stroma of tarsus containing large number of hyaline pink staining masses (amyloid material by special staining) some of which show calcium deposits. Stroma shows intense collection of chronic inflammatory cells. mag 21x.



FIG 6 The same case under high power 60x. Hyaline amyloid material is well seen.



FIG 7 (M. I.) Amyloidosis with chronic inflammatory cells 60x. Shows that tarsal tissue has almost completely undergone amyloid change containing a few hyaline concretions. Scattered cross collagen fibres are seen in stroma which contains chronic inflammatory cells especially plasma cells.



FIG 8 (M.) Amyloidosis post trachoma 21x. The section shows extensive amyloid change in the tarsal tissue including changes in the blood vessels. There is tendency towards formation of pseudo-glands probably due to proliferation of the lining epithelium. There is chronic inflammatory reaction and a degenerated lymphoid follicle under the epithelium.

narrowing of the palpebral fissure (Fig 4b) In some cases it was difficult even to evert the upper lid The corner was usually normal or showed ghost vessels of old trichoma Later on bulbar conjunctiva, caruncle and semilunar folds also became affected (Fig 2) In four of the early cases no mention is made about trichoma in the records



FIG 2 Amyloidosis affecting the lower lid with involvement of the bulbar conjunctiva



FIG 3 Amyloidosis affecting both the lids



FIG 4a Amyloidosis affecting the upper lid of the right eye



FIG 4b Amyloidosis affecting the upper lid of the right eye with narrowing of the palpebral fissure

# HISTOLOGICAL EXAMINATION

All the cases were confirmed by histological examination. In some cases the lid structure with its epithelium and follicles etc could be recognised while in other cases the whole tissue had undergone massive amyloid change. In the fibrous stroma there could be seen a few criss cross collagen fibres and a few chronic inflammatory cells that is lymphocytes, plasma cells (5 cases) and occasional foreign body giant cell (3 cases). Special staining for amyloid material (Iodine and Congo red etc) was done in most of the cases. The blood vessels particularly arteries, showed amyloid infiltration with end arteritis and thickened media. In some cases mucous glands dilated with calcified concretions were seen. Evidence of scarring and degenerated lymphoid follicles under the epithelium pointed out to the fact that they were post trachomatous. Histological reports of six cases were as follows —

*Case No 2 — R L 22 years Hindu female*

Section showed irregular pieces of tissue. These pieces consisted of irregular pink staining hyaline material (staining positive for amyloid) in which occasional stray spindle shaped cells were seen at the periphery. A few lymphocytes and plasma cells were scattered throughout the tissue. No stratified squamous epithelium or other epithelial structures of the lid were seen.

## Diagnosis Amyloid Disease of Lid

*Case No 5 — S S 32 years Sikh male*

Both the sections presented similar appearances. They showed masses of hyaline pink staining material with focal collections of chronic inflammatory cells and a few blood vessels. At places these cell collections enclosed a few foreign body giant cells. Special staining was positive for amyloid material.

## Diagnosis Amyloid Deposit Eyelid

*Case No 9 — S R 29 years Hindu male*

All the biopsy pieces were covered superficially by squamous epithelium of the conjunctiva. In the sub epithelial region there were hyaline pink masses which were structureless. A few connective tissue strands, fine blood vessels and collections of plasma cells were interspersed in between them. The walls of the vessels were impregnated with similar material. This material stained positively for amyloid substance.

*Case No 10 — M P 20 years Hindu male*

The section showed fibro-collagenous stroma of the tarsus containing a large number of hyaline pink staining masses which were



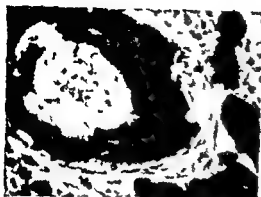


FIG. 9 The same under high power 140x



FIG. 10 (J) Amyloidosis post trachomatous 60x The section is lined by squamous epithelium. The sub-epithelial tissue shows infiltration with chronic inflammatory cells and the rest shows deposit of amyloid material. This area is also rich in blood vessels probably indicating that amyloid degeneration has occurred after granulomatous reaction in the tissue.

FIG. 11 (A R) The section (Mag 60x) shows amyloid degeneration in tarsal plate forming homogeneous eosinophilic masses. The blood vessels do not show much amyloid changes. The infiltration with cells is also scanty (Primary amyloidosis).



and is diagnostic and typical. In other cases definite trachomatous scarring was encountered.

Out of our eight recent cases four of them confirmed and admitted that they had also passed through the same second stage for a long period before treatment was sought. So we suggest that those patients of trachoma who suffer from a prolonged second stage are more predisposed to amyloidosis than others.

Laboratory investigations were not of much help. Differential and total WBC counts, W R, Kahn test, urine, stools, conjunctival smears tests contributed little. Blood cholesterol values were estimated in only 7 cases and were within normal limits. The liver, spleen, kidneys and cardiovascular system were normal in all cases.

**HISTOLOGICAL EXAMINATION**

All the cases were confirmed by histological examination. In some cases the lid structure with its epithelium and follicles etc could be recognised while in other cases the whole tissue had undergone massive amyloid change. In the fibrous stroma there could be seen a few criss cross collagen fibres and a few chronic inflammatory cells that are lymphocytes plasma cells (5 cases) and occasional foreign body giant cell (3 cases). Special staining for amyloid material (Iodine and Congo red etc) was done in most of the cases. The blood vessels particularly arteries showed amyloid infiltration with end arteritis and thickened media. In some cases mucous glands dilated with calcified concretions were seen. Evidence of scarring and degenerated lymphoid follicles under the epithelium pointed out to the fact that they were post trachomatous. Histological reports of six cases were as follows —

*Case No 2 — R L, 22 years Hindu female*

Section showed irregular pieces of tissue. These pieces consisted of irregular pink staining hyaline material (staining positive for amyloid) in which occasional stray spindle shaped cells were seen at the periphery. A few lymphocytes and plasma cells were scattered throughout the tissue. No stratified squamous epithelium or other epithelial structures of the lid were seen.

**Diagnosis Amyloid Disease of Lid***Case No 5 — S S, 32 years Sikh male*

Both the sections presented similar appearances. They showed masses of hyaline pink staining material with focal collections of chronic inflammatory cells and a few blood vessels. At places these cell collections enclosed a few foreign body giant cells. Special staining was positive for amyloid material.

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*Case No 10 — M P 20 years Hindu male*

The section showed fibro collagenous stroma of the tarsus containing a large number of hyaline pink staining masses which were

irregularly distributed. A number of these masses showed deposits of calcium. No bony trabeculae were discernible. The stroma showed intense collection of chronic inflammatory cells. Special staining showed the hyaline masses to be amyloid (Figs 5 and 6).

### **Diagnosis Amyloid Tumour of the Lid**

*Case No 13 — J, 14 years, Hindu male*

The tissue was covered by squamous epithelium. The subepithelial tissue was infiltrated with chronic inflammatory cells and beneath the epithelium there was a deposit of amyloid material. This area was also rich in blood vessels, thereby indicating amyloid degeneration following granulomatous reaction in the tissue (Fig 10).

### **Diagnosis Amyloidosis—Post Trachomatous**

*Case No 14 — M, 38 years, Mohamedan male*

#### **MUSHTAQ AHMAD 38 MOHAMEDAN MALE**

The section showed that the tissue had undergone amyloid change for the most part. Hyaline concretions were also seen. There were stray collections of chronic inflammatory cells, specially the plasma cells. Von Gieson stain showed a few criss cross collagen fibres, while the rest had undergone amyloid degeneration. Methyl violet stain showed metachromasia of the homogeneous amyloid mass (Fig 7).

### **Anatomical Diagnosis Amyloidosis—Post Trachomatous**

*Case No 15 — I R, 42 years, Mohamedan male*

The section showed the tarsal plate to be most affected by amyloid degeneration in the form of homogeneous eosinophilic masses while this change was not prominent in the blood vessels. The amyloid material had taken a bright khaki stain with Von Gieson and showed metachromasia with Methyl violet stain (Fig 11).

### **Anatomical Diagnosis Amyloidosis—Primary**

*Case No 16 — M, 22 years Hindu male*

The section showed that the tissue for the most part had undergone amyloid changes. The blood vessels also showed amyloid degeneration. There was little normal glandular tissue remaining probably as a result of the proliferation of the hanging epithelium to form pseudoglands. There was infiltration with chronic inflammatory cells and at one place a degenerated lymphoid follicle under the epithelium (Figs 8 and 9).

### **Anatomical Diagnosis Amyloidosis—Post Trachomatous**

#### **TREATMENT**

The growth should be removed together with the tarsal conjunctiva and tarsal plate leaving only 1 to 2 mm near the lid margin.

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(Tarsectomy) The remaining tarsal plate is then sutured to the conjunctiva and levator muscle near the fornix by three double armed sutures (Modified Blasovics operation) If the bulbar conjunctiva is involved it has to be slowly dissected and shelled out as the growth is subconjunctival The raw areas can be repaired by mucus membrane grafts from the lip The pieces of friable tissues should be carefully removed because if some portions are left they have tendency to redevelop as occurred in three of our cases, one of which had been operated upon about ten years previously Recurrences have been reported by Duggan and Chitnits (1950) hence post operative radio therapy is further suggested (Redi 1949) We have tried Beta therapy 6000-9000 rep by strontium 90 applicator

### SUMMARY

Amyloidosis of the conjunctiva is more common than generally suggested It may be primary but most of the cases occur in areas where trachoma is predominant and are secondary to the chronic irritation which is a sequel to this disease It is suggested that those cases which have a prolonged untreated second stage of the papillary hypertrophy type are probably more predisposed to amyloidosis 21 investigated cases found in our records of the past 7½ years are reviewed As after excision the possibility of a recurrence cannot be ruled out it is further suggested to give beta therapy in such cases

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## OPERATIVE TREATMENT OF XEROPHTHALMIA BY TRANSPLANTATION OF DUCTUS STENONI INTO CONJUNCTIVAL SAC

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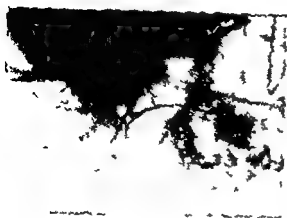
For many centuries physicians had no means to provide permanent moistening of the xerophthalmic eye and the patients with xerophthalmia were condemned to agonizing blindness.

In 1951 the author proposed a surgical method of treatment of xerophthalmia which consists in displacement of ductus Stenoni into the conjunctival sac. The approach to the sac is effected by a cut through skin. In the same year Filatov and Shevlev independently of the author also proposed the transplantation of ductus Stenoni separating the latter in the substance of the cheek through a cut in the mucous membrane of the mouth. For the past eleven years the operation done mostly by our method received a wide support. On the subject there was much written in the Soviet and foreign press.

In the process of elaborating the method we have introduced different modifications that have simplified the technique of operation which considerably increased number of persons who could undergo it.

Our research made on healthy persons by means of contrast X-ray of ductus Stenoni (sialography), showed that the duct is long enough to be displaced into the conjunctival sac only in half of the cases. We have in mind here not so much the absolute length of the duct as the length useful in the transplantation, that is the linear distance from the outlet of the duct at the gland to the corner of the eye. This simple computation should be made before the operation (2) (2a). When preliminary sialography shows absolute or relative insufficiency of the duct we lengthen the latter to the necessary size by means of a tube formed from the mucous membrane of the cheek (3).

The operation itself consists in a skin cut corresponding to the duct projection: 1) its delicate separation together with an area of mucous membrane (round or square) surrounding the orifice of the duct (4). Form and size of the resected mucous membrane depend on the necessary lengthening of the duct. If there are additional branches of the duct they are severed and tied. To make the final separation of the duct easier we introduced two instruments. One is a round or a rectangular protruder that is put on the duct; it pushes the mucous membrane of the mouth out and the other is a large diameter trephine that easily resects the mucous membrane. (5-6).



2 Contrast X Ray photo of the ductus stenom

2a A Diagram of computation of the duct length necessary for its displacement to the eyeball



3 Lengthening of the duct

### *Lengthening of the duct*

After the separation of the duct the hole in the mouth is sutured (8). Then four holder sutures are applied to the resected mucous membrane surrounding the orifice of the duct (7). From the operation wound in the cheek an underskin tunnel opening into the conjunctival sac at the outer corner is made with a wide slit knife. The holder sutures are then taken by long thin pincers that are passed through the tunnel (7) and the sutures are pulled through it to be sewn to the conjunctiva of the lower fornix. If the conjunctival sac is insufficient it can be increased by the mucous graft from the mouth. To prohibit infection the cheek is infiltrated with a solution of antibiotics.

Up to now we have performed thirty three operation on the eyes of patients with severe xerophthalmia. A positive result was





FIG 1 A patient before operation. A line of dissection is marked according to sialography findings



FIG 7 Ductus Stenosi has been freed with the surrounding mucous of the cheek.



FIG 8 A hole in the mucous of the cheek after separation of the duct

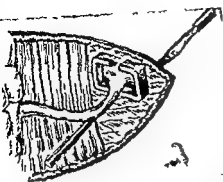


FIG 4 The duct bluntly separated from the surrounding tissue. A rubber strip is placed under it



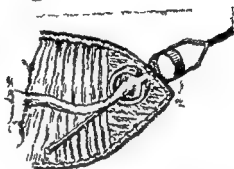
FIG 9 Forming of the underground tunnel and stretching of the duct to the eye by holder stitches.





5 A Rectangular Protruder at work (a diagram)

6 Round protruder and knife at work (a diagram)



obtained in thirty cases. The most frequent complications encountered by us were infection (three cases), downward displacement of the duct (two cases) and temporary ceasing of gland function, probably due to trauma of nerve fibres. When the duct slips out of the conjunctival fornix a cut in skin is made at the lower margin of the orbit and the duct sutured again.

We have satisfied ourselves that serous saliva offers excellent tear substituting fluid. This can be explained by its great chemical and physical closeness to the tears. The eye excellently stands the operation. Vototic patches usually disappear or diminish in the very first few days. Also there is a large decrease in the number of keratic cells in the scrapings of the conjunctiva. In some cases separate dry areas persist. This can be ascribed to great trophic changes in the basal epithelium. The patients cease to feel the tormenting dryness. In most cases the acuity of vision is increased. The moistened eyes can undergo optical operations (transplantation of cornea, iridectomy, etc.) well.

The only defect of the new operation is the flow of saliva during taking of food. There were several methods proposed for elimination of the excessive salivation: severing of nerve auricle temporalis, conjunctiva anastomosis (Bennet), partial resection of parotid gland. We have successfully irradiated parotid gland (single dose of 120r to 150r. Total dose being 600r to 1500r controlling the therapeutic effect by Schirmer's test).

## ETIOLOGICAL PROBLEMS IN UVEITIS

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Every ophthalmologist is able to settle the diagnosis of uveitis on the spot and he usually starts treating it immediately. But in most cases this treatment will be purely symptomatic.

We usually assume that uveitis is an inflammatory disease and at the same time we think of a reaction between some unknown antigen and a specific antibody. This reaction sets free histamine like products causing inflammation. Anti-allergic drugs and steroids will certainly influence this reaction but will never reveal the etiology.

Many attempts have been undertaken to demonstrate specific antigen in the diseased eye, be it bacterial, viral or a parasitic. Positive results for about every possible infective agent have been reported in the literature, but mainly on enucleated eyes. These findings are very important for our knowledge of endogenous eye diseases, but this kind of investigation did never have much clinical value. The percentage of positive results is much too low, most cases remain unsolved problems.

We have therefore paid more attention to the detection of specific antibodies in the eye. It must be said that despite the great work of I. C. Woods there is no reason to believe that a specific infection in the eye leads to an increase of specific antibodies in the blood or to an increased sensitivity of the skin. Very recent studies of Hallett, Wolkowicz, Faria, Leopold and Wjczyski and also of Coles have shown, that blood tests alone (Middlebrook Dubos Test for Tbc, Antistreptolysine O Test) are of no value in the diagnosis of uveitis cases. It is therefore very strange that everybody still believes very much in the diagnostical value of the Dye test (Sabin Feldmann) for the detection of toxoplasmosis. One should be aware that all these tests be it blood tests or skin tests can only be conclusive if they are negative. Then at least we know, that this kind of infection is very unlikely to be the cause of an eye infection.

We can assume that for practical purposes, a local antigen antibody reaction within the eye leads to a surplus of antibody. This antibody will most certainly remain fixed within the tissue. But part of it will leak into the blood stream, and part of it may get into the intraocular fluids (vitreous, aqueous humour). If we can determine these antibodies quantitatively within the blood, and at the same

## EXPERIMENTAL ASPECTS OF EALES'S DISEASE

By RYUTARO HAGINO

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In spite of the fact that 80 years have passed since the first description of Eales's disease by Henry Eales the etiology, methods of treatment and prophylaxis related to it have not yet sufficiently elucidated. It is not even certain as to what the complete definition of this disease is. Consequently it may be supposed that etiology of this disease is not easily defined by the experimental methods heretofore studied using of clinical cases.

### CLINICAL ASPECTS

In the present studies statistical analysis were carried out in 133 cases of recurrent intraocular hemorrhage in which definitely diagnosed systematic diseases were not included. The age of the patients was generally young covering from 15 to 58 but most fell in the younger category of 15 to 35 (Table 1). Out of 133 cases, 103 were male and 30 female. The right eye was affected in 51, left eye in 46 and both in 36 eyes.

The important diseases in the patients' past histories include lung tuberculosis, rheumatism, constipation, epistaxis, icterus, kidney disease, gastroptosis, anal fistula, hookworm disease, anaemia, tonsilitis and so on. As eye complications, uveitis, iridocyclitis, cataract and glaucoma were observed. The skin tuberculin test was positive in 40 and negative in 9 of the 51 patients which showed accurate clinical history in the card, and 21 patients out of 133 had long tuberculosis in their past histories (Table 2).

Besides these 133 patients the author observed a few cases who had clinical entity like Eales's disease and had both primary retinal and retino vitreous hemorrhage in old age. That is uncertain whether or not these cases should be classified as Eales's disease or whether there must be further elucidation.

Also from the standpoint of classification it may be supposed that some cases might develop from different cause e.g. previous case, Buerger's disease, sepsis and anaemia even though tuberculous symptoms existed were proved in the greater number of cases. Consequently in the studies of Eales's disease a more thorough examination of the etiology is first problem to be solved and clinical explanation, especially problems of the treatment may be of secondary consideration.

TABLE 1 *Distribution of age in 133 cases of Eales's disease*

Age	Male		Female		Total	
	No of Cases	% of Cases	No of Cases	% of Cases	No of Cases	% of Cases
15~19	13	13.8	8	26.7	21	20.3
20~24	18	14.3	4	13.3	22	13.8
25~29	33	29.4	5	16.7	38	23.1
30~34	14	11.6	6	20.0	20	15.8
35~39	8	9.2	2	6.7	10	7.9
40~44	5	7.3	2	6.7	7	7.0
45~50	6	6.3	0	0.0	6	3.2
50~54	5	5.9	2	6.7	7	6.3
55→	1	2.0	1	3.3	2	2.6
Total	103	100.0	30	100.0	133	100.0

TABLE 2 *Tuberculin Test in 51 cases of Eales's disease*

	(-)	(±)	(+)	(++)	Total
Male	7	2	23	9	41
Female	2	0	7	1	10
Total	9	2	30	10	51

#### STUDIES ON CONSTITUTION OF THE BLOOD IN THE PATIENT OF EALES'S DISEASE

The experiments were carried out to study the portent of the change of blood of patients in the mechanism of hemorrhage.

Injection of patient serum into the vitreous body of the rabbit. Since Oguchi's first description many students have tried the same experiments to elucidate the onset of retinitis proliferans.

In the present studies autoblood was injected into vitreous of the same rabbit both in complete blood and separated components *e.g.* red blood cells, white blood cells, serum and hemoglobin.

The results obtained from this experiment duplicated the many changes as appeared in previous literatures, showing the dilatation of vessels, fibroblasts and sprouting capillaries which invaded the vitreous from the retina the changes of outer layer of the retina, and so on. As the most marked change a substance like ceroid pigment was observed in Oil red O stained specimen.

**Fibrinolysin in the blood or in the vessel wall tissues.** The studies on fibrinolysin in the blood of Eales's disease are still unsettled. In the present experiments the author suspected the existence of some relationships between the retinal hemorrhage and fibrinolysin in the blood or in the vessel wall tissues and from this standpoint proteinase capillary permeability promoting action and capillary resistance were measured.

In the results obtained the above three factors proved markedly positive during a bleeding attack but all these phenomena do not always appear and neither they are characteristic of Eales's disease (Table 3).

With this experimental fact in mind serum was obtained during a retinal hemorrhage was experimentally injected into rabbit vitreous and that in turn caused retinal and vitreous hemorrhage.

The results are very important because it shows presence of some substances in the serum which plays an important role in a retinal hemorrhage.

#### STUDIES ON RETINAL AND VITREOUS HEMORRHAGE USING DEAD BCG VACCINES

As mentioned above the etiology of Eales's disease is not yet decided but a large number of the cases were elucidated as tuberculosis or tubercular allergy. Many experimental studies were carried out to solve this question using live tubercle bacilli. In the present studies the author tried to explain it by dead BCG vaccines.

#### EXPERIMENTAL METHODS

Dead BCG vaccine was made by the following methods. BCG vaccine was suspended into physiological solution of sodium chloride and killed by steamheating at 100°C for 30 minutes in Koch's steam sterilizer.

The experimental methods were carried out as follows: (1) Injection of dead BCG vaccines into the common carotid artery. (2) Injection of the vaccines into the rabbit vitreous body. (3) Injection of the vaccines into the carotid artery and at the same time into the vitreous. (4) Injection of the vaccines into the auricular vein. These procedures were carried out on sensitized and non sensitized rabbits.

The results obtained. In the non sensitized rabbits with dead BCG vaccine injection into carotid artery spotted hemorrhages in the peripheral retina were observed 3 days after injection. Retinal vessels dilated a little and sometimes projected into the vitreous. These

TABLE 1 Distribution of age in 133 cases of Eyle's disease

Age	Male		Female		Total	
	% of Cases	No. of Cases	% of Cases	No. of Cases	% of Cases	No. of Cases
15~19	13	13	8	26	21	20
20~24	18	14	4	13	22	13
25~29	33	29	5	16	33	23
30~34	14	11	6	20	20	10
35~39	8	9	2	6	10	7
40~44	5	7	2	6	7	7
45~49	6	6	0	0	6	3
50~54	5	5	2	6	7	6
55+	1	2	1	3	2	2
Total	103	100	30	100	133	100

TABLE 2 Tuberculin Test in 51 cases of Eyle's disease

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TABLE 3 Fibrinolysis in the Blood in the patient of Eales's disease

No of Cases	Age Sex	Diagnosis	Recurrents of Hemorrhage	Cr	F	C P P			Note
						> 25	> 50	× 100	
1	33	Control		—	—	6 × 5	5 × 5	4 × 4	Pregnancy 8 Mon 5 Days before the Hemorrhage In the Midst of H 7 Days before the Hemorrhage In the Midst of H 3 Days after the Hemorrhage 3 Days after the Hemorrhage Epistaxis Epistaxis and Anal Bleeding 2 Days after this procedure
2	25	Control		—	+	8 × 8	6 × 6	5 × 4	
3	26	Control		—	—	5 × 5	5 × 4	3 × 3	
4	23	R V H	3	—	+	9 × 8	6 × 6	5 × 5	
5	32	V O & H	1	±	+	8 × 7	8 × 7	6 × 6	
6	35	R V H	1	±	+	5 × 4	5 × 4	1 × 1	
7	40	R V H	1	±	+	8 × 8	6 × 5	4 × 3	
8	20	R V H	2	+	±	11 × 9	8 × 7	8 × 6	Pregnancy 8 Mon 5 Days before the Hemorrhage In the Midst of H 7 Days before the Hemorrhage In the Midst of H 3 Days after the Hemorrhage 3 Days after the Hemorrhage Epistaxis Epistaxis and Anal Bleeding 2 Days after this procedure
			2	—	+	6 × 6	5 × 4	3 × 3	
			3	+	+	6 × 6	4 × 4	3 × 3	
			3	—	+	6 × 5	5 × 4	4 × 3	
9	27	R V H	1	—	+	9 × 8	8 × 7	7 × 6	
10	23	Periphrictitis		+	+	9 × 8	8 × 7	6 × 6	
11	16	R V H	2	+	+	10 × 9	9 × 9	9 × 9	

R V H Retinal and Vitreous Hemorrhage

V O &amp; H Vitreous Opacity and Vitreous Hemorrhage

Cr Capillary Resistance

F

Fibrinolysis

C P P

Capillary Permeability Promoting Action

retinal changes by intravitreal injection were more marked than these of the former method

The following results were obtained in sensitized rabbits. First sensitization method. Dried BCG vaccine was suspended into physiological solution of sodium chloride and inoculated intracutaneously

1st injection	0.25 mg/0.2 cc
2nd injection	0.5 mg/0.2 cc
3rd injection	0.75 mg/0.2 cc

In this experiment the hemorrhages on the papilla surface of the rabbit were seen 12 days after a carotid artery injection

Next pathological observations. The changes of the retina, retinal vessels, choroid and vitreous body were observed respectively. Especially hemorrhage lesions seen with the naked eye were caused by rupture of the retinal vessels or sprouting capillaries. Moreover marked retinal changes and cell infiltration in choroidal tissues were observed (Fig. 1)

When it was injected into auricular vein, no retinal hemorrhage or other retinal changes were observed

The injection of dead BCG vaccines proved that peripheral hemorrhages, vascular changes and proliferated changes of the retina were caused by that procedure on non-sensitized rabbits (Fig. 2). However, in the sensitized animals retinal hemorrhages were observed at central area and on the surface of the papilla (Fig. 3). The mechanism of hemorrhage is supposed to have a relationship with rupture of the vessel walls or diapedesis.

In intravenously injected cases vitreous body became cloudy on the day following injection, so that the hemorrhage was visible in the retina, but by the histopathological study many other marked changes were revealed. There were wandering cells, proliferation of the tissues, cell infiltration surrounding the vessels and sprouting capillaries (Fig. 4 & 5).

From these results it is presumed that the hemorrhage and recurrent hemorrhage have some association with allergic or pre-allergic state.

#### EXPERIMENTAL STUDIES ON HEMORRHAGE OF THE RETINA AND VITREOUS BODY WITH HYDRODYNAMIC METHOD AND SNAKE VENOM

Mizuno et al. studied on fragilities of retinal vascular system by hydrodynamic method and then by a vascular tree specimen by Häuser and Sibay's technique. From this experiment it was revealed that arteries show no changes, but vein of the retina is weaker than that of the brain (Fig. 6).

Studies on hemorrhage with snake venom

To begin with a minimum dose inducing hemorrhage was measured and it was decided that density over 0.5/0.2 cc was necessary to bleed.

TABLE 3 Fibrinolysin in the Blood in the patient of Eales's disease

No of Cases	Age Sex	Diagnosis	Recurrents of Hemorrhage	Cr	F	C P P			Note
						/ 25	> 50	> 100	
1	33	Control		-	-	6 / 5	5 < 5	4 < 4	Pregnancy 8 Mon 5 Days before the Hemorrhage In the Midst of H 7 Days before the Hemorrhage In the Midst of H 3 Days after the Hemorrhage 3 Days after the Hemorrhage Epistaxis Epistaxis and Anal Bleeding 2 Days after this procedure
2	25	Control		+	+	8 < 8	6 < 6	5 < 4	
3	26	Control		-	-	5 < 5	5 / 4	3 / 3	
4	23	R V H	3	-	+	9 < 8	6 / 6	5 / 5	
5	32	V O & H	1	±	+	8 < 8	8 > 7	6 < 6	
6	35	R V H	1	±	+	5 < 4	5 < 4	1 < 1	
7	40	R V H	1	±	+	8 / 8	6 / 5	4 / 3	
8	20	R V H	2 2	+	±	11 / 9 6 > 6	8 / 7 5 > 4	8 < 6 3 > 3	
9	27	R V H	3 3	+	+	6 < 6 6 > 5	4 / 4 5 > 4	3 > 3 4 < 3	
10	23	Peripblebitis R V H	1	-	+	9 / 8	8 > 7	7 < 6	
11	16		2	+	+	9 / 8 10 > 9	8 / 7 9 / 9	6 > 6 9 / 9	

R V H Retinal and Vitreous Hemorrhage  
V O & H Vitreous Opacity and Vitreous Hemorrhage  
Cr Capillary Resistance F Fibrinolysin C P P Capillary Permeability Promoting Action



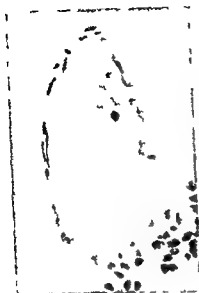


FIG 5 (Hagino and Tamura) Eosinophilic leukocytes in the blood of the retinal vein 3 days after the injection of dead BCG vaccines into the carotid artery (Non sensitized rabbit H E stain  $\times 800$ ) Same animal as in Figure 2

FIG 6 (Mizuno Miyata and Tamura) Dilating venula by the hydrodynamic method Equator area of the retinal vessels (Young cat vascular tree specimen  $\times 60$ )



FIG 7 (Mizuno Miyata and Tamura) The disorganized reticular structure in the outside of the venula with the intravitreous injection of snake venom (Young cat vascular tree specimen  $\times 600$ )



FIG 1 (Hagino and Tamura) The part of marked retinal changes and cell infiltration in choroidal tissues 12 days after the injection of dead BCG vaccines into the carotid artery (Sensitized rabbit H E stain  $\times 200$ )

FIG 2 (Hagino and Tamura) Hemorrhages vascular changes and proliferated changes of the peripheral retina 3 days after the injection of dead BCG vaccines into the carotid artery (Non sensitized rabbit H E stain  $\times 800$ )

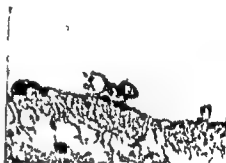


FIG 3 (Hagino and Tamura) Hemorrhages on the surface of the papilla 12 days after the injection of dead BCG vaccines into the carotid artery (Sensitized rabbit H I stain  $\times 280$ ) Same rabbit as in Figure 1

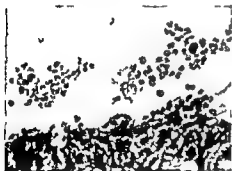


FIG 4 (Hagino and Tamura) Hyalinosis of the part of the retinal vein (Non sensitized rabbit H E stain  $\times 800$ ) Same rabbit as in Figure 2



The results obtained In all cases just after injection the retina became anaemic, and the papilla pale In 5-20 minutes the blood current became visible while the arteries continued their contraction, and the veins dilated

After that various changes appeared e.g. luxation of lens cataract and glaucoma Next retinal haemorrhages began to appear on the surface of papilla or its surrounding area and gradually hemorrhages expanded to peripheral vessels especially to veins (Fig 9) The changes of the fundus differ from each other according to experimental condition of injected substances

Histo pathological findings Blood and wandering cells were observed on the surface of the papilla Besides the arteries swelled and were surrounded by eosinophil leucocytes, the vein dilated and became thinner

In peripheral retina there were haemorrhagic lesions caused by rupture of the vessels Generally retinal changes were more remarkable in neuroepithelial layer but brain layer stayed almost intact In the changes noted after 15 days the papilla looked like choked disc

The clinical and pathological findings above noted were observed in the cases were injected 1000 u/0.1 cc solution of  $\alpha$  chymotrypsin (Fig 10)

In the cases of 500 u/0.1 cc 6 hours after injection the vessels on the surface of papilla seemed to be in pre bleeding state and suffered from eosinophil leucocytes (Fig 11)

In the peripheral area of retinal haemorrhages were proved to exist which should have been caused by rupture of the vessel walls In this case also thrombus formation was observed (Fig 12)

In the case of 50 unit injection haemorrhages were also observed in peripheral area and also thrombus formation 15 days later haemorrhages disappeared spontaneously In the case in which 1 unit was injected only wandering of red blood cells was proved as changed condition after 15 hours

From the results noted above it was well clarified that for the studies of retinal haemorrhage adequate dose of  $\alpha$  chymotrypsin should be from 10-15 u/0.1 cc Moreover it is notable phenomenon that retinal haemorrhage appears in nasal side and it recurs This problem is not yet elucidated

#### STUDIES ON RETINAL HAEMORRHAGE WITH $\alpha$ AMINOCAPROIC ACID

Recently aminocaproic acid is used in order to stanch in clinic for the reason that this substance inhibits activation of enzyme However if  $\alpha$  aminocaproic acid is administered continuously fibrinolysin becomes voluminous or is activated against such substance The present studies were carried out to elucidate the relationship between a function of proteinase and its inhibitor



So 200, 50, 5, 0.5/0.2 cc snake venom solution were injected into rabbit vitreous body, respectively. After injection retinal haemorrhaging began at different times according to density of venom. In the beginning spotted haemorrhages appeared on the surface of papilla and its surroundings, and gradually increased. Then the haemorrhages were observed at peripheral vessels. During 1-2 hours haemorrhagic area expanded and at the same time more vitreous haemorrhages were observed.

**Histo pathological findings.** Generally venule is more invaded than arteriole. In PAS staining of the arteriolar walls they are very similar to those of normal vessel, but venule walls stain unevenly. Moreover nucleus shows karyolysis or nuclear swelling. In some lesions, rupture of vessel walls and haemorrhages are revealed.

In the next experiments 5 and 0.5/0.2 cc snake venom were injected into young cat vitreous. Time duration of bleeding in cat is longer than that of rabbit. Haemorrhages first appeared in spots at equatorial area and gradually increased in number and extended, resulting in vitreous bleeding. Furthermore, those haemorrhages appear along the veins. Vascular system surrounding the papilla shows no marked changes, but at peripheral area reticular structure present in the outside of vein is lost and shows homogenous structure and varicose like structure. Capillaries lost normal anastomosis, showed marked meandering and the wall became thinner (Fig. 7).

**Histo pathological findings.** Marked haemorrhages were seen between inner limiting membrane and ganglionic cell layer. The wall of venule became remarkably thin. Nucleus showed vacuolization and in some area no polysaccharide staining was observed. Moreover, ganglionic cell layer was markedly destroyed (Fig. 8).

The results obtained by injection of snake venom into crotalid artery differed from these by the former method. Particularly no changes were observed in veins.

In previous experiments, the following facts were elucidated. The tissue changes caused by venom attack from outside were more remarkable than these from inside of vessel wall. Fragilities of venule and capillaries were caused only by invasion from outside.

It is well known fact that the influences of snake venom on the vein wall should be caused mainly by activity of proteinase. In the present experiment it was suspected that the retinal vein was affected more easily from outside.

#### STUDIES ON RETINAL HEMORRHAGE WITH $\alpha$ CHYMOTRYPSIN

**Experimental methods.**  $\alpha$  chymotrypsin solution of 1000 u/0.1 cc 500 u/0.1 cc, 5 u/0.1 cc, 1 u/0.1 cc respectively was injected into rabbit vitreous body. Observation was carried out in two groups one from 6-15 hours after injection, and the other from 15-25 days after.

The results obtained. In all cases just after injection the retina became anaemic, and the papilla pale. In 5-20 minutes the blood current became visible while the arteries continued their contraction, and the veins dilated.

After that various changes appeared e.g. luxation of lens, cataract and glaucoma. Next retinal haemorrhages began to appear on the surface of papilla or its surrounding area and gradually haemorrhages expanded to peripheral vessels especially to veins (Fig. 9). The changes of the fundus differ from each other according to experimental condition of injected substances.

Histopathological findings. Blood and wandering cells were observed on the surface of the papilla. Besides, the arteries swelled and were surrounded by eosinophil leucocytes, the vein dilated and became thinner.

In peripheral retina there were haemorrhagic lesions caused by rupture of the vessels. Generally retinal changes were more remarkable in neuroepithelial layer but brain layer stayed almost intact. In the changes noted after 15 days the papilla looked like choked disc.

The clinical and pathological findings above noted were observed in the cases where injected 1000 u/0.1 cc solution of  $\alpha$ -chymotrypsin (Fig. 10).

In the cases of 500 u/0.1 cc 6 hours after injection the vessels on the surface of papilla seemed to be in pre-bleeding state and suffered from eosinophil leucocytes (Fig. 11).

In the peripheral area of retinal haemorrhages were proved to exist which should have been caused by rupture of the vessel walls. In this case also thrombus formation was observed (Fig. 12).

In the case of 50 unit injection haemorrhages were also observed in peripheral area and also thrombus formation. 15 days later haemorrhages disappeared spontaneously. In the case in which 1 unit was injected only wandering of red blood cells was proved as changed condition after 15 hours.

From the results noted above it was well clarified that for the studies of retinal haemorrhage adequate dose of  $\alpha$ -chymotrypsin should be from 10-15 u/0.1 cc. Moreover it is notable phenomenon that retinal haemorrhage appears in nasal side and it recurs. This problem is not yet elucidated.

#### STUDIES ON RETINAL HAEMORRHAGE WITH $\alpha$ -AMINOCAPROIC ACID

Recently  $\alpha$ -aminocaproic acid is used in order to stanch in clinic for the reason that this substance inhibits activation of enzyme. However if  $\alpha$ -aminocaproic acid is administered continuously, fibrinolysin becomes voluminous or is activated against such substance. The present studies were carried out to elucidate the relationship between a function of proteinase and its inhibitor.



FIG 8 (Mizuno Miyata and Tamura) Retinal haemorrhages with the intravitreal injection of snake venom (Young cat H E stain,  $\times 280$ )

FIG 9 (Hagino and Tamura) Fundus photograph of the retinal haemorrhage in the peripheral areas 3 days after the intravitreal injection of  $\alpha$  chymotrypsin (50 u/0.1 cc) (Colored rabbit)

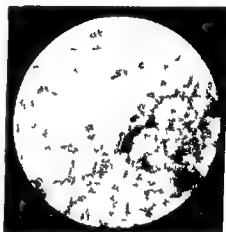


FIG 10 (Hagino and Tamura) Retinal haemorrhage on the surface of the papilla or its surrounding area and marked changes of the vessels 6 hrs after the intravitreal injection of  $\alpha$  chymotrypsin (1000 u/0.1 cc) (Colored rabbit H E stain  $\times 600$ )



FIG 11 (Hagino and Tamura) Pre bleeding state with eosinophilic leukocyte infiltration 6 hrs after the intravitreal injection of  $\alpha$  chymotrypsin (500 u/0.1 cc) (Colored rabbit H E stain  $\times 200$ )





FIG 12 (Hagino and Tamura) Haemorrhages and thrombus formation of the retinal vessels 3 days after the intravitreal injection of  $\alpha$ -chymotrypsin (500 u/g 1 cc) (Colored rabbit H E stain  $\times 500$ )

FIG 13 (Hagino and Tamura) Fundus photograph of retinal haemorrhage in the peripheral areas 2 days after the intravitreal injection of  $\epsilon$ -aminocaproic acid (0.01 g/g 1 cc) (Albino rabbit)



FIG 14 (Hagino and Tamura) Haemorrhage in the peripheral retina 2 days after the intravitreal injection of  $\epsilon$ -aminocaproic acid (0.01 g/g 1 cc) (Albino rabbit H E stain  $\times 280$ )

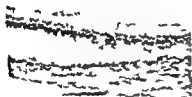


FIG 15 (Hagino and Tamura) Vascular tree of the hemorrhage in the retinal capillaries 2 days after the intravitreal injection of  $\epsilon$ -aminocaproic acid Same rabbit as in Figure 13

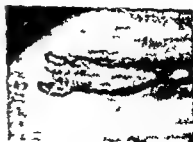




FIG 8 (Mizuno Miyata and Tamura) Retinal hemorrhages with the intravitreal injection of snake venom (Young cat H F strain  $\times 280$ )

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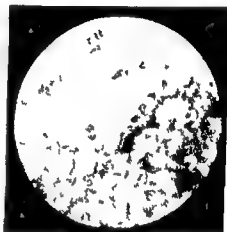


FIG 10 (Hagino and Tamura) Retinal hemorrhage on the surface of the papilla or its surrounding area and marked changes of the vessels 6 hrs after the intravitreal injection of  $\alpha$  chymotrypsin (1000 u/0.1 cc) (Colored rabbit H E stain  $\times 600$ )



FIG 11 (Hagino and Tamura) Pre-bleeding state with eosinophilic leukocyte infiltration 6 hrs after the intravitreal injection of  $\alpha$  chymotrypsin (500 u/0.1 cc) (Colored rabbit H E stain  $\times 200$ )





FIG 12 (Hagino and Tamura) Haemorrhages and thrombus formation of the retinal vessels 3 days after the intravitreal injection of  $\alpha$ -chymotrypsin (500 u/0.1 cc) (Colored rabbit H.E. stain  $\times 1500$ )

FIG 13 (Hagino and Tamura) Fundus photograph of retinal haemorrhage in the peripheral areas 2 days after the intravitreal injection of  $\epsilon$ -aminocaproic acid (0.07 g/1 cc) (Albino rabbit)



FIG 14 (Hagino and Tamura) Haemorrhage in the peripheral retina 2 days after the intravitreal injection of  $\epsilon$ -aminocaproic acid (0.07 g/0.1 cc) (Albino rabbit H.E. stain  $\times 280$ )



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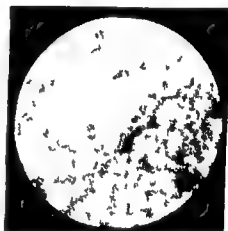


FIG 10 (Hagino and Tamura) Retinal haemorrhage on the surface of the papilla or its surrounding area and marked changes of the vessels 6 hrs after the intravitreous injection of  $\alpha$ -chymotrypsin (1000 u/0.1 cc) (Colored rabbit H F strain  $\times 600$ )



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Especially tuberculous changes constitute one of important factors as etiologic condition of Eales's disease

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**Experimental methods** 0.02g/0.1 cc solution of  $\alpha$ -aminocaproic acid was injected into vitreous body of the rabbit 3 days later China ink was injected into the auricular vein of the same rabbit

Just after injection slight dilatation of retinal vein was observed 2 days later capillary haemorrhages of the retina appeared (Fig. 13) 3 days later extended specimen of the retina was made from the rabbit injected 10 cc China ink By studies on this vascular tree specimen spot shaped haemorrhages of the retina were noticed (Fig. 14, 15)

Of the results obtained it may be supposed that activation of proteinase also is induced by injection of enzyme inhibitor

# COMMENT AND SUMMARY

Nowadays the etiology of Lales's disease is still not defined clearly, and at the same time it is neither clear that what clinical findings are included in this disease Consequently, experimental studies on this disease revealed various difficulties to settle experimental signs Actually the studies are not rare, but most of them are limited to clinical field

In the present studies the mechanism of retinal and vitreous haemorrhages was selected as the first thing to be solved To attain this object the studies on the characteristic blood structure of the patient, structure of retinal vessel walls and studies on influences of various enzymes on the vessel were carried out using different experimental methods From these experiments a number of suspected problems could have been solved

During the retinal haemorrhage, fibrinolysis in the blood is activated, and at the same time capillary permeability promoting action becomes stronger On the other hand, retinal hemorrhage by the intravitreal injection of patient's serum of Lales's disease has been detected Other experiments were tried to clarify the meaning of the walls of the retinal vessel on haemorrhage For this purpose the experiments noted above were carried out using snake venom,  $\alpha$ -chymotrypsin Or  $\alpha$ -aminocaproic acid

The results obtained show that there is a definite relationship between activation of proteinase in the walls of retinal vessel and retinal haemorrhages As it is well known, blood pressure of the retinal capillary is high and moreover, resistance in the walls of the retinal veins is weaker than that in the brain Accordingly, when the walls were influenced from some disease, for example from tuberculosis retinal haemorrhages would be induced easily just like Lales's disease

As noted in the opening paragraph it is known that there are various kinds of clinical type in recurring intraocular haemorrhage caused by indefinite etiology Therefore, the mechanism of retinal haemorrhage was analysed in various ways and it was concluded that the structure of vascular walls and the components of the blood might play an important role

From these clinical and histopathological findings, it may be supposed that the haemorrhages are caused from various factors

tary tract the cardiovascular, urinary hematopoietic and other systems and that it damages the connective tissues and is responsible for a multiplicity of cutaneous disorders. The role played by tuberculin type hypersensitivity and chronic infection is an important one for it can enormously intensify tissue damage and destruction. It is well known that the local hypersensitivity response to tuberculo protein antigen in this type of hypersensitivity is delayed and prolonged. The prevention of the hypersensitivity reaction by desensitization with old tuberculin is now rarely done because of the risk of general and focal reactions.

If the inflammation in the wall of the peripheral veins in the eye is due to a hypersensitivity to tuberculo protein antigen, then the cortico steroids may reduce the allergic reaction as long as therapy is continued. It has been experimentally demonstrated that the beneficial effects of steroid therapy are mainly due to an ability to block the tissue reaction to hypersensitivity.

Since 1944 the author has had the opportunity to study in detail approximately 60 patients with Eales's disease. Most of these patients were young adult males veterans of World War II, and were under periodic observation in a large veterans' hospital. Many of them were examined two and three times a year over this period. Evidence of healed or active pulmonary tuberculosis was present in approximately one third of the cases and the skin tuberculin test was positive in almost all the patients. From this experience it is felt that there are two clinical aspects of the medical treatment of Eales's disease. The first is the initial treatment of the vitreous haemorrhage or when a subsequent vitreous haemorrhage occurs. The second aspect of the medical treatment is the management of the lesions in the retinal veins and the newly formed capillaries aneurysms etc. which are formed usually in the periphery of the retina.

#### GENERAL DISCUSSION OF MEDICAL THERAPY

There is no specific treatment known for Eales's disease. Most frequently these patients have been treated in the past as if they were tuberculous by tuberculin desensitization injections and general hygienic measures. However further haemorrhages have frequently occurred during the course of tuberculin therapy probably from focal reactions and this form of treatment has not met with uniform success or acceptance. The author has experienced such reactions in several patients in whom massive vitreous haemorrhages occurred following a tuberculin injection. In Donders' (4) comprehensive survey of the entire literature on Eales's disease in 1958 he concludes that there is no certain medical therapy.

The specific anti tuberculous drugs do not seem indicated such as thiazolsulfone (Promisole R) streptomycin para aminosalicylic acid and isoniazid because of the apparent lack of active bacterial tuberculous infection in Eales's disease. The author treated two cases for prolonged periods in hospital with anti tuberculous chemotherapy and in both

## MEDICAL THERAPY OF EALES'S DISEASE\*

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Although the condition known as Eales's disease is generally thought to be rare there are few among us who have not had several of these patients to treat and the question of these recurrent hemorrhages into the vitreous frequently proves vexing. The general concepts of Eales's disease, experimental production of the disease, etiological pathological concepts, surgical therapy and prognosis are being discussed by other members of the symposium. The medical therapy which one employs will be dependent upon one's concept of the etiology of this disease.

The history and findings are so similar that the author (1, 2) concluded the disease should be considered a clinical entity and not a manifestation of many diseased conditions. There are haemorrhages from the peripheral retinal veins, perivascular exudation alongside the walls of the veins and, in many instances, haemorrhages into the vitreous. It was postulated that the haemorrhages and exudation resulted from a local hypersensitivity reaction in the walls of the peripheral retinal veins in individuals who have been sensitized to tuberculo protein antigen.

Three eyes were available for pathologic study. Two had been removed when the patient died from tuberculosis and one when glaucoma supervened. In the latter case no signs of perivascular inflammatory process were found, while in the first two eyes a non-specific lymphocytic cuffing was noted. Study of the pathologic material revealed that some of the retinal vessels were surrounded by a few lymphocytes but on the whole there was little, if any, inflammatory reaction around the vessels. A true inflammatory periphlebitis was not present. There were no granulomatous reactions around the vessels and no tubercle bacilli were found in the studies with specific staining. The pathologic findings were compatible with the hypothesis that the disease has an allergic basis.

Rich (3) has demonstrated that the hypersensitivity state can produce serious disturbances in the respiratory tract and in the skin.

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\* Read at the VII International Congress of Ophthalmology, New Delhi Symposium on Eales's Disease, December 5th, 1962.

\*\* From the Department of Ophthalmology, University of British Columbia and the Department of Ophthalmology, Shaughnessy Hospital, Department of Veterans Affairs, Vancouver, British Columbia, Canada.

In certain patients where the vitreous haemorrhage does not absorb sufficiently within months consideration may be given to vitreous replacement according to the method of Shafer (10). The author has used this treatment in several patients with remarkable success and for no explainable reason with equal failure in others with the onset of phthisis bulbi.

(b) *Management of Lesions in the Retinal Veins After Absorption of Vitreous Haemorrhage*

In this stage of Eales's disease the author has advocated the use of subconjunctival injections every two or three months of steroid cortisone, hydrocortisone acetate or prednisolone 25 mg in 1 cc. The patients selected for this treatment were those who showed signs of activity of the periphlebitis in whom retinal haemorrhages could be observed ophthalmoscopically in the periphery of the retina. As long as haemorrhages in the retina were noted the disease was considered to be active but when haemorrhages did not occur the condition was thought to be inactive. As many as eighteen subconjunctival injections have been made in a single eye over a four year period without ill effect. It was observed that the steroid usually required two to three months to become absorbed from beneath the conjunctiva but in some patients the residue deposit would be absorbed in five to six weeks.

The author has advocated the use of subconjunctival injections of steroid locally in order to reduce the possibility of flaring up an inactive systemic pulmonary tuberculous infection. He has felt that the local use of steroid subconjunctivally probably suppresses the allergic response in the walls of the peripheral retinal veins. This opinion was supported by the clinical observations in these patients in whom no further vitreous haemorrhages occurred in the majority of patients so treated. Periodic observation is necessary in order to determine if the lesions are proliferating with gradual enlargement of newly formed venous aneurysms in patients with Eales's disease. This type of case is the phase of the disease probably most satisfactorily treated by photocoagulation.

During the past two years the associates of the author at the Banting Institute University of Toronto have been studying experimentally the total ocular uptake and routes of penetration of C(14) labelled hydrocortisone following subconjunctival administration in an attempt to determine the depth of penetration and amount of drug taken up by the individual layers of the eye and also the manner of spread from the depot site. These studies are being carried out in rabbits by Drs Basu, Gornall, Wine and Drysdale, and are currently underway. The preliminary observations indicate that only a very small amount of the subconjunctival depot of steroid actually enters the eye. Disappearance of the steroid deposit from the subconjunctival location appears to occur within seven days. The studies are being continued with the development of a radio autographic technique to visualize the route of penetration into the eye and its tissue locali-

patients recurrent vitreous haemorrhages occurred while on maximal chemotherapy medication. Hogan, (5) in a personal report, studied eight patients with long term anti tuberculous chemotherapy without noting any improvement in the condition.

Many other methods of medical therapy have been advocated for Eales's disease, including potassium iodide orally or intravenously as sodium iodide, proteolytic enzymes, thyroid extract, and estrogenic hormones as well as androgenic hormones, all of which the author does not advocate. Ascorbic acid has been advocated by many authors as well as rutin and dicoumarol. The choline derivatives are considered to have a lipotropic effect on tubercle bacilli and an anti-haemorrhagic effect but opinions about its value are most uncertain. The use of cobra venom is also open to differing opinions.

Radiation therapy to the posterior segment of the eye has been employed by numerous authors (6, 7). Reese and Jones (8) report favorable results in an eight and ten year follow up of patients with Eales's disease treated by roentgen therapy. However, the author treated two patients with roentgen therapy with doubtful success.

#### SPECIFIC TREATMENT OF EALES'S DISEASE

##### (a) *Treatment of the Patient with a Vitreous Haemorrhage*

Usually the patient first presents himself at the time of the initial spontaneous vitreous haemorrhage. As is well known, these patients are usually in good health. However, a complete medical examination is indicated, including X ray examination of the chest, skin tuberculin test, complete blood studies, especially in regard to sickle cell anemia, neurological examination and peripheral vascular studies regarding the possibility of Buerger's disease.

The author feels that a patient with vitreous haemorrhage should be admitted to hospital for complete bed rest and the eyes relatively immobilized either with bandages or pin hole spectacles. Given optimal conditions the vitreous haemorrhage is likely to largely absorb relatively quickly with the rapid return of normal central vision. The haemorrhage will settle to the lower portion of the vitreous and within one to two weeks the fresh haemorrhage changes in appearance and there are many flocculent appearing white opacities in the inferior portion of the vitreous. If there are no signs of active systemic tuberculosis on careful medical examination, the author advocates intensive ACTH therapy intravenously over a ten day to two week period while the patient is in bed in hospital. Twenty to thirty mg ACTH in 500cc of distilled water are administered intravenously by means of a slow drip over a five to eight hour period each day. With the absorption of the vitreous haemorrhage a careful ophthalmoscopic examination usually reveals the site of the haemorrhage to be from a peripheral or mid peripheral retinal vein. Should a subsequent vitreous haemorrhage occur, the patient is re-admitted to hospital and the course of ACTH therapy repeated in order to provide maximal block of the hyper sensitivity state to tuberculo protein antigen.

## TRANSCLERAL DIATHERMIC COAGULATION IN EALES'S DISEASE

A. FRANCESCHETTI

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We have been using surface diathermocoagulation in the treatment of Eales's disease at the Geneva Clinic since 1947. We adopted this procedure for two reasons: first because all medical treatment suggested had proved inefficient in most instances. This is hardly surprising in view of the lack of accurate knowledge as to the etiology of the disease. This holds true for all disorders in which the patient's condition and constitution seem to play the most important role as in our opinion is the case in Eales's disease.

The second reason was the high success registered by Wess (1939) with diathermic coagulation in the treatment of angiomas of the retina and certain chronic peripheral retinitides (probably including some benign cases of Eales's disease).

On several occasions we have had the opportunity of speaking about the results obtained by this new technique which gradually caught on such an extent that the destruction of retinal foci in haemorrhages into the vitreous of young patients regardless of the method used has now become the therapy choice (Franceschetti, A and Forni, S, 1954; Franceschetti, A 1955; Franceschetti, A and Forni, S 1954; Forni, S 1938; Ricci, A 1959).

Since Meyer Schuickeraath (1956) developed his remarkable instrument a few years ago, we have been able to destroy affected areas by photocoagulation.

The time has come to attempt a definition of the indications and possibly the advantages of one or the other of these two operative techniques.

The principal merit of photocoagulation is accuracy. It therefore offers the advantage of making it possible to limit destruction sharply and to approach the central area without great risk of jeopardizing sight. It is of incontestable utility in dealing with the insufficiencies which may appear at the edge of diathermically coagulated areas.

Moreover, it is the only method by which vessels in the vitreous can be destroyed.

We reserve diathermy for

(a) the coagulation of extensive areas

If an entire quadrant or the entire periphery is to be destroyed, we consider that diathermy has the advantage of simplicity, speed and,

zation Of major interest is whether the steroid can actually diffuse through sclera underlying the depot site into the individual ocular layers

## CONCLUSIONS

- 1 There is no specific medical cure known for Eales's disease at the present time
- 2 The author is of the opinion that the disease is a manifestation of allergy to tuberculo protein antigen elsewhere in the body
- 3 Medical treatment basically should be directed towards blocking this hypersensitivity state The judicious use of steroid therapy either locally or systemically seems a rational way of attempting to accomplish this end
- 4 Further experimental studies are necessary in order to determine whether subconjunctival depots of steroid actually diffuse through the sclera and are capable of blocking locally the hypersensitivity state in the wall of the peripheral retinal veins

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We reserve diathermy for

(a) the coagulation of extensive areas

If an entire quadrant or the entire periphery is to be destroyed, we consider that diathermy has the advantage of simplicity, speed and

if appropriately carried out, above all of generally causing relatively few secondary reactions and, in particular far less exudative phenomena

(b) *the coagulation of peripheral areas*

It is often difficult to focus on these areas with the photocoagulator and it is therefore to achieve far easier coagulation diathermically

(c) *the coagulation of detached areas*

For which there is an absolute contraindication to photocoagulation which, for physical reasons, cannot be achieved

(d) *coagulation under unfavourable visibility conditions*

Because of a cloudy vitreous, exudates for which the sight accuracy of photocoagulation cannot be justified or applied

(e) *patients who have not the possibility to be under regular control*

These cases have in general a bad prognosis as photocoagulation will not be done in time if near areas are affected. On the contrary, extended diathermocoagulation prevents in general recurrent haemorrhages

(f) *overcast skies "coagulation (coagulation "a ciel couvert")*

In extensive haemorrhage into the vitreous where destruction of entire suspected areas as well as an attempt to improve resorption of the haemorrhage are indicated. The technique itself is not new and is closely related to that for detachment of the retina, however, with the important reservation that the zones to be coagulated, after exact localization, can be very slightly parchmented, if necessary, under ophthalmoscopic control. With very weak intensities, there is always a whitish exudate sometimes bordered by minute haemorrhages which resorb and have no tendency to invade the vitreous. The after effects of the operation are always extremely slight. Important post operative measures are keeping both eyes bandaged for five days and bed rest.

Although in performing the overcast skies operation coagulation more often than not covers and extensive area about 14 mm from the limbus, we always try to base our procedure both on the case history and on whatever information the patient's regular ophthalmologist may be able to supply concerning the main location of the lesions at the time when it was still possible to explore the fundus. We have already cited the happy turn events may take with this procedure. Evidently there is sometimes a direct relation between diathermic coagulation and the rapid clearing up the vitreous, which had often remained opaque for several months. Very often, within a few days after the operation, the fundus becomes visible and in favourable cases, patients recuperate sufficient visual acuity.

In 1958 we cited three similar cases. Since then, in ten cases where there was perception of light, this procedure resulted in five instances in rapid resorption of the blood exudates in the vitreous body.

*Scientific symposia and symposia read at the XIX International Congress of  
Ophthalmology held at Delhi from 2nd December to 7th December 1962*

PRINTED IN INDIA

BY PYARELAL SAH AT THE TIMES OF INDIA PRESS BOMBAY AND EDITED AND  
PUBLISHED BY DR Y A C PANDIT BOMBAY MUTUAL BUILDING  
SIR PHIROZ HAH MEHTA ROAD BOMBAY

Forgacs an assistant at the Geneva Clinic studied the effect of surface diathermocoagulation on the resorption of intra vitreous haemorrhages on rabbits. These experiments which will be published shortly confirm clinical observations. Although the action of diathermocoagulation was not determined Forgacs was able to demonstrate the same phenomenon as observed in man. It should be pointed out that we distinguish between two types of treatment prophylactic in which diathermy is applied to lesions which have not yet caused haemorrhages into the vitreous and therapeutic intended for more serious cases in which haemorrhage has already occurred. With present techniques it is obvious that prophylaxis will, more often than not be reserved for photocoagulation whereas therapy will most often make use of diathermocoagulation.

Thus prior to 1959 we had treated 6 cases prophylactically with diathermy five successfully as confirmed by time. Since then cases of this type have been reserved for photocoagulation.

Our statistics since 1947 comprise 48 cases covering 64 eye operations.

Diathermy was applied 46 times and photocoagulation alone or combined with diathermy was used for the remainder.

We will conclude by noting once more that the destruction of affected areas in Eales's disease appears to us to be the only method at present offering satisfactory encouraging results. Results would probably be better still if on appearance of the symptoms use were made of these techniques which up to present time have proved absolutely safe.

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# ERLES'S DISEASE TREATMENT WITH LIGHT-COAGULATION

G MEYER-SCHWICKERATH

*Essen Germany*

Encouraged by reports of VFRHOEFF and FRANGLSCHITTI on the favourable influence of diathermy coagulation in Erles's Disease I started light coagulation treatment in 1954. Since then 139 patients (176 eyes) have been treated.

## TECHNIQUE OF TREATMENT AND NORMAL FOLLOW UP

The technique of treatment has altered during the course of time. I shall now describe it in the same way as it is carried out today.

The pupil is maximally dilated and the eye is anesthetized by means of a retrobulbar injection of 5 cc Novocain with hyaluronidase. All aneurysms and newly formed vessels must be coagulated. They can often only be seen at first in their actual extension during light coagulation. We therefore make a new sketch after this treatment in which the coagulated vessels are recorded. Fortunately the changes in the vessels, above all in the early stages, lie in the periphery of the retina, so that the resulting defect in the visual field is only small. The coagulation is easy if the vessels lie in the level of the retina and are not covered with exudate or hemorrhage. It is dangerous and unnecessary to coagulate the dilated and curved vessels, which end in peripheral aneurysms and coils of vessels. After the coagulation of the aneurysms these vessels resume their normal structure. In cases of proliferation of vessel-trees into the vitreous one can try to close off the arterial and venous roots of these trees by coagulation.

The intensity of the light coagulation can be especially low in cases of Erles's Disease. It is mostly enough if less than the basic power I, is used, i.e. that the iris diaphragm is closed for some degrees. The intensity is sufficient when, in half a second, a faint whitish colouring of the retina in the region of the vessels occurs. The vessels themselves hardly change their appearance at all. First in the course of 2-3 weeks one recognizes whether they are completely closed and have been resorbed.

After 4-6 weeks we make another thorough examination in order to see whether any aneurysms are still visible. If this is the case, these changes have to be treated again with light coagulation.

As a rule we coagulate not more than one quarter of the retinal circumference. If larger regions in the periphery of the retina are

affected then we leave an interval of 2 weeks between each coagulation treatment

The further course is marked by the fact that smooth vessel free scars develop in the coagulated region. The retinal vessels leading to the scars have a normal size and a normal course. After the coagulation of all visible aneurysms has been carried out, check up examinations are made from time to time. If new proliferations take place these will again be treated. They often occur in regions of vessels which one would least suspect but hardly ever in the region of the old scars.

#### STATISTICS OF CASES

The following statistics contain also cases from the first years in which we had very little experience and in which coagulation was insufficient — according to our opinion today. There are also cases in which only a part of the peripheral vessel changes was visible and coagulated whereas others were completely hidden by haemorrhage.

During the time from March 1954 until the end of June 1961 (1954–1959 in Bonn 1959–1961 in Essen) 139 patients (i.e. 176 eyes) with Eales's Disease were treated with light coagulation. Out of these we could follow the course of 114 patients (22 women and 92 men), i.e. 146 eyes. In 3 eyes light coagulation was used to heal a detachment due to Eales's Disease. There remain therefore only 143 eyes.

67% of the patients were bilaterally affected (DODEN gives 70%).

27 patients were blind in one eye from the same disease and 5 patients from other or unknown causes.

In 99 eyes one or several severe vitreous haemorrhages had occurred before the treatment.

16 patients had an *iritis* earlier or one which was still persistent during the treatment.

The number of light coagulation treatments carried out is

in 71 eyes	1 session
in 38 eyes	2 sessions
in 22 eyes	3 sessions
in 12 eyes	4–8 sessions maximum

During an observation period of 1 year minimum 8 years maximum average period 2.9 years 124 out of 143 treated eyes remained without further haemorrhages.

Out of the 124 symptom free eyes there are 12 with a decrease in visual acuity due to traction and exudative degenerative processes in the region of the macula and one eye with a dense cataract behind which the retinal process most probably has settled down.

The 19 eyes in which further symptoms occurred are on the whole very severe and progressive cases. Mostly the aneurysmal changes

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FIG 4 The same area as Fig 3 6 weeks after photocoagulation The coagulated aneurysms are replaced by a smooth scar which is nearly free of vessels A comparison with Fig 2 and 3 shows that the enlarged feeding vessels regained a normal calibre

of the periphery had already advanced very far almost to the centre or there were extensive proliferations into the vitreous

### Complications

#### (1) HAEMORRHAGES

Haemorrhages occurring during coagulation can mostly be brought to a standstill by immediate coagulation of the blood 4 severe vitreous haemorrhages occurred during the coagulation and could not be stopped They have all been resorbed except in one case There were five small vitreous haemorrhages during the first week after the treatment In all cases a quick resorption followed

Smaller pre retinal haemorrhages can be very often seen in the first two weeks after light coagulation It is often only due to the absorption of the coagulated aneurysm

Other haemorrhages which have occurred through new non coagulated aneurysms or due to insufficient coagulation are not mentioned here They are considered under the failures

#### (2) RETINAL DETACHMENT

A detachment of the retina was seen nine times during or after the treatment with light coagulation With the exception of one case we are dealing with very progressive cases with vitreous tractions





FIG 1 Arterious venous net work 3 days after photocoagulation



FIG 2 Typical appearance of Exudative Disease in the temporo-superior periphery with aneurysms and short cuts



FIG 3 The same area as FIG 2 4 days after photocoagulation

We presume that abnormal development of vessels is present also in Coats's disease and in Miliary Aneurysms Retinitis. These two diseases are also progressive and sometimes accompanied by an iritis. In early stages the affected vessels can be destroyed by light coagulation and thus the disease is brought to a standstill.

### Summary

Encouraged by VERHOFF'S and FRANCESCHETTI'S reports on the favourable influence of diathermy coagulation in Eales's disease I have treated 139 patients, i.e. 176 eyes with light-coagulation from 1954 to 1961.

Out of 143 eyes whose course could be followed over an average of 2.9 years 124 eyes remained without any new haemorrhages.

Experience has shown after destroying the vessel proliferations and arterio-venous aneurysms that not only any haemorrhage is missing but that also the tendency to new proliferations disappears in the region of the coagulated vessel.

Observations of the first apparent stages have shown that the disease begins with dilated arterio-venous vessels (shunt-capillaries) in the peripheral retina. The process proceeds by development of further arterio-venous aneurysms from the periphery in the direction of the center of the retina. It leaves behind a vessel free region in the peripheral retina. The ophthalmoscopic observations may be explained by the fact that a capillary closing process (in outbursts) is the beginning of the disease which may be embolic, thrombotic or of endangitic nature. This progresses independently further through a circulus vitiosus between hypoxaemia and vessel proliferation.

The favorable influence of light coagulation can only be explained in the following way: that the circulus vitiosus is interrupted by the destroyed aneurysms and/or that the resulting scars do not give any fresh stimulation for proliferation of new vessels.

The coagulation of aneurysms cannot hinder the fact that new proliferations occur in other vessel regions previously unaffected. These must be coagulated again in order to prevent fresh haemorrhages.

In the treatment of Eales's disease by light-coagulation different complications occur (haemorrhages, detachments, macular degenerations) which obviously cannot always be avoided.

In spite of these complications I would like to recommend light-coagulation therapy in Eales's disease. It leads in most cases to a clinical cure of this disease.

and proliferations. Three cases could be re-attached by scleral resection and 1 case by girdle suture.

In 8 eyes there was a retinal detachment before the treatment. In 6 eyes the operation was a success so that they could be followed by coagulation of the aneurysms.

From this number it follows that the operative prognosis of detachment due to Eales's disease has improved since we have treated these cases by volume reducing operations.

### (3) POSTCOAGULATIVE MACULAR DEGENERATIONS

This peculiar macular process occurred not only in patients with Eales's disease but also in others, which have been treated by diathermy or light coagulation for other reasons. This disease has been known for a long time as the so called "distance injury" of the macula after diathermy operation. R. BRÜCKNER has recently reported on an interesting observation concerning this.

The process begins mostly a few weeks up to two months after light coagulation has been carried out. Sometimes the visual acuity improves after antiphlogistical therapy with Cortison, Butazolidin or Tanderil. In many cases there still remains a large permanent central scotoma. We experienced these complications 5 times in a severe form (visual acuity less than 5/50) and 4 times in a less severe form (visual acuity better than 5/50).

This complication is the more serious because in all cases it does not concern a very advanced or complicated form. In all cases the visual acuity was normal or practically normal before the treatment.

How can one explain the surprising effect of light coagulation in Eales's disease?

The sickle cell hemoglobin Cretinopathy shows us that quite a similar process may arise through multiple microemboli. It seems to be possible that an obliterating or obstruting process in the shunt capillaries of the peripheral retina appears also at the beginning of the so called Eales's disease. This process once brought into action could become independent and then progress in a circulus vitiosus of hypoxiemie and proliferation from the periphery to the centre. The circulus vitiosus will be interrupted by the coagulation of the aneurysms. At the same time a scar tissue with a low oxygen supply is developed. The inflammatory and degenerative appearances characterizing the later stages of the disease should only then be considered as the consequence of an disturbed hemodynamic.

Developmental anomalies of retinal vessels, especially in the peripheral retina, can obviously bring into action quite a similar picture.

It is well-known, that the clinical picture of the Varix Aneurysmaticus Retinae may proceed and lead to a similar final stage as in Eales's disease. We have observed 4 cases of this type.

- 5 Syphilis — only two patients out of 100 had this lesion which was coincident. It does not cause haemorrhage though it involves every structure of the body including eye. Rather it causes endarteritis obliterans.
- 6 Anaemia — none of our patients had anaemia of a severe degree to cause haemorrhage.
- 7 Malaria — The disease in our country is definitely on decrease and is not restricted to males.
- 8 Blood calcium deficiency — only 2 cases had low blood calcium.
- 9 Environmental disturbances — This is the result and not the cause of the disease.
- 10 Tubercular periphlebitis.
- 11 Endocrinal disturbances.
- 12 Retinal perivasculitis.

In my opinion the lesion is caused by allergy due to tuberculo proteins. The positive skin Tuberculin Test in patients is more worthy in view of survey of tuberculin tests in younger adults of comparable age group which indicate that only 25 to 40% cases are positive. It seems that the patient with recurrent intra ocular haemorrhage has become sensitized to Tuberculo proteins and a local state of hypersensitivity has developed in the walls of retinal veins with resultant exudation and haemorrhage.

Regarding mode of infection reaching the eye, the infection travels through the blood vessels and the organism penetrates through the small arterioles reaching the perivascular tissues of small veins to cause periphlebitis. In my opinion the infection gets lodged in the ciliary body where it reaches via blood stream and either the bacteria themselves or the toxins produced by them pass via the vitreous to act upon the blood vessels causing periphlebitis.

I do not think that local retinal perivasculitis at the periphery causing neovascularization which may be inter retinal, uveal or vitreal can explain the course of events leading to rupture causing recurrent intra-ocular haemorrhage. It was present only in 12 out of 100 cases.

As to why the condition is rare in females than in males 1 to 25 can not be explained by above etiology as tubercular periphlebitis and retinal perivasculitis are quite common in them.

Glandular disturbances may be playing an important role about which we know very little.

#### FAMILY HISTORY

Only 6 patients gave positive history of tuberculosis in the family stating that their parents were admitted in T B sanatorium.

## EAL'S DISEASE—ITS ETIOLOGY & PROGNOSIS

Dr S P GUPTA, F.R.C.S., (Ldin), D.O.M.S., (Lond),  
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The following conclusions have been derived from 100 cases of Eales's disease treated privately and in King George's Medical College, Lucknow

### INCIDENCE

The disease though world wide is more common in tropics and in our series average age was 23.9 years youngest in a child aged 15 years and eldest male 48 years

It is more common in males than females ratio in my series is 25 to 1. Mostly patients belonged to low income group were field workers and were of active habits. Out of our series of 100 cases of Eales's disease the classification is as follows

Field workers	40
Clerks	20
Students	20 (3 were medical students)
Businessmen	10
Policemen	6
Housewives	4
	<hr/> 100 <hr/>

### ETIOLOGY

A large number of conditions have been mentioned as the cause of Eales's disease

- 1 Akin to thrombo angitis obliterans or erythema nodosum
- 2 Septic foci in teeth, tonsils or other parts of Body
- 3 Helmentiasis — 50% of cases mostly field workers and clerks had ankylostomiasis infection. This is very common in our country chiefly in those residing in rural areas or in unhygienic conditions in the urban areas
- 4 Vitamin deficiency — none of vitamin deficiency is directly or indirectly related to this condition

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Out of these 84 cases reported sudden loss of vision and 16 cases only gradual loss of vision

Only 12 cases out of 100 showed neo vascularization

Above cases were divided for treatment in three broad groups with complete rest in bed

- 1 50 Cases treated by antitubercular treatment consisting of Dihydrostreptomycin 1 gm O.D. for 1 month, Tibizide 50 mgm B.D. for one month, and subconjunctival streptomycin 1 cc twice a week
- 2 25 Cases put on coagulant therapy consisting of Calcium gluconate with vitamin C 10% 10 cc A.D. such 15 Hemostic tab or Stryptobion or Claudin } 1 Tab B.D.
- 3 25 Cases put on endocrinal therapy — Testosterone Propionate starting with 5 mgm increased to 10 mgms on alternate days intra muscular for one month

I have not tried light coagulation therapy

We found that patients put on anti tubercular treatment with subconjunctival streptomycin behaved better and only in 6 cases recurrence was present. Of course anti tubercular treatment should be repeated after every 4 months. Such three courses should be given and patient advised to carry on light work and not do manual work.

Prognosis will also depend on the stage at which patient has presented himself first time and the period that has elapsed before the treatment has been started. We have found that prognosis was worse in cases which had recurrent haemorrhage or which presented themselves with old iridocyclitis chorio retinitis or where retinal detachment has occurred due to formation of fibrous bands (Retinitis Proliferans). The younger the age of patients worse was the prognosis.

The prognosis was better in cases put on anti tubercular treatment with subconjunctival treatment repeated after 4 months. Very few cases presented themselves with Retinal perivascularitis and no haemorrhage. I have no experience of light coagulation therapy which is still not much in use in our country as treatment of Eales's disease.

**FURTHER INVESTIGATIONS**

W R and Kahn positive in 2 out of 100 cases blood calcium, Blood Serum, prothrombine normal except in 1 case

Urine, W B C count, haemoglobin and differential count normal examination of Stool (revealed ankylostomiasis infection in 50 cases)

Sinuses were normal except in 1 case

Only 3 eyes were enucleated as the eyes were blind

Histopathological examination revealed tubercular lesions, — epitheloid and giant cells

Constipation and headache does not seem to be important features of the disease

Though Henry Eals laid great stress on it and he did so to bring the symptomatology of the disease in line with hypothesis of alimentary and circulatory neurosis. Probably his patients were cases of sinus trouble or other conditions giving rise to headache which is quite common

The mental state being in low spirits seems natural in a young man whose visual acuity in either or both eyes is being repeatedly interfered with and each time going down due to irreversible changes

A young man with prospects of living in this world without good vision will not keep himself in high spirits. This was clearly noticed in three medical students who became neurotic and in low spirits with each attack of haemorrhage. In my series of cases none had high blood pressure

**FIRST EYE AFFECTED**

In our series right eye was affected in 66 and left eye in 34 cases. Eighty of them took treatment as soon as first eye got affected, all of them reported for check up. Second eye was not affected in these cases. In twenty cases other eye was affected the interval being 6 months to 2 years

The recurrence has no relation with the eyes which got first affected. Sometimes the eye which was affected first showed less recurrence than the eye that was affected late. Eighty four cases reported sudden loss of vision

**MANIFESTATIONS—ITS RELATION TO PROGNOSIS****Review of 100 Cases**

- 1 Usually the patients manifest first with periphlebitis and retinal and vitreal haemorrhage — 8½ cases
- 2 Manifest as branch venous thrombosis leading to haemorrhage — 10 cases
- 3 Manifest as chronic iridocyclitis or chorio retinitis and then leading to vitreous haemorrhage — 6 cases

The table indicates that about  $3/4$  of all the eyes can be saved in this way. In addition it demonstrates, that light coagulation in Eales's disease gives the best results when performed during the initial stages of its development. Under these conditions there were only few failures in relation to the successful cases, viz 4 against 23, i.e. 1/6 in the first group. This correlation decreases in the second group, here were 4 failures to 14 good cases, i.e. about 1/3.5. In the third group are found 6 failures against 4 cured cases, this corresponds a relationship of 1/0.66. In this latter group the failures predominate remarkably.

It is to be concluded therefore that light coagulation as treatment of Eales's disease should be done as early as possible. The practical value and importance of light coagulation in Eales's disease may also be demonstrated by the following history. A young man suffering from bilateral Eales's disease (group I) was coagulated on his right eye and was considered to be cured over more than one year. Unfortunately, he refused the treatment on his left eye and the left eye is now blind by recurrent hæmorrhages.

One of our advanced cases had a delayed hæmorrhage in the vitreous and two had delayed retinal detachment. In the early stages however we could find no complications which would contraindicate light coagulation as a treatment of choice in that otherwise hopeless disease.

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## SIGNIFICATION DE LA POLYGLOBULIE ET DE L'HYPERCOAGULABILITE DANS LA PATHOGENIE ET LE TRAITEMENT DE LA MALADIE d'EALES

JOSÉ CASANOVAS

(Barcelona)

En collaboration avec Mrs Castillo Farreras et Olivella nous avons démontré la grande fréquence de la polyglobulie dans la périphlébite rétinienne. Sur 59 patients 28 c'est à dire la plus grande partie avaient plus de 5 millions d'hématies par centimètre cube. Les valeurs de l'hématocrite étaient souvent altérées, on trouvait habituellement la vitesse de sédimentation globulaire diminuée, fait normal dans les polyglobulies mais apparemment paradoxal chez les malades qui souffraient un processus inflammatoire actif.

Dans la production des thromboses en général peuvent intervenir l'hypercoagulabilité, l'estase et les altérations de la paroi vasculaire. Dans les thrombophlébites rétiniennes du syndrome d'Eales interviennent surtout les altérations vasculaires (périphlébite et phlébite). Bien que, dans quelques cas l'hypercoagulabilité ne soit pas le facteur pathogénique le plus important toutefois, il reste le plus accessible

## DISCUSSION

### TREATMENT OF EALES'S DISEASE BY LIGHT COAGULATION

W BÖKE,  
(Germany, Munster Westf)

There is no doubt, that light coagulation is a unique and effective method of treating Eales's disease. May I give some personal experience and results with it over the past four years, including a total number of 55 eyes in 43 patients. Post operative observation was maintained in 53 eyes and all the cases were classified in 3 groups according to the severity of disease as viewed by ophthalmoscopy.

The *first group* was called "initial alterations", i.e. small haemorrhage spots and exudates along the retinal veins, dilatation and tortuosity of the peripheral vessels and new formed retinal vessels as well.

*Group No. 2* consists of the retinal features of group No. 1 plus the additional findings of recurrent vitreous haemorrhage.

The *third group* were the poor cases, wherein we found the characteristics of group No. 2 complicated by neovascularization of the vitreous, retinal detachment or secondary glaucoma.

The end result is as follows

	Eyes	+	(+)	-	?
Group I	27	22	1	4	—
Group II	18	10	4	3	1
Group III	10	2	2	5	1
	55	34	7	12	2
		41		14	

- + = absolutely successful cases i.e. practically healed cases without recurrences  
 (+) = good results remarkable improvement the final result however, is not yet sure  
 - = no success recurrent haemorrhages neovascularization of the vitreous retinal detachment etc  
 ? = patients did not return for follow up studies

The table indicates that about  $3/4$  of all the eyes can be saved in this way. In addition it demonstrates that light coagulation in Eales's disease gives the best results when performed during the initial stages of its development. Under these conditions there were only few failures in relation to the successful cases, viz 4 against 23 or 15% in the first group. This correlation decreases in the second group: here were 4 failures to 14 good cases, i.e. about 1/3.5. In the third group are found 6 failures against 4 cured cases: this corresponds a relationship of 1/0.66. In this latter group the failures predominate remarkably.

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One of our advanced cases had a delayed hæmorrhage in the vitreous and two had delayed retinal detachment. In the early stages however we could find no complications which would contraindicate light coagulation as a treatment of choice in that otherwise hopeless disease.

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Le traitement par le Sintrom sous contrôle a duré de 5 à 30 mois (en moyenne 14). Si nous comparons ces résultats avec ceux du groupe traité par médication anticoagulante nous obtenons les résultats suivants

	Nombre de cas	Echecs	Cas restés stationnaires	Améliorations	Pourcentage des améliorations
Sans traitement anticoagulant	36	5	7	24	60 %
Avec traitement anticoagulant	10	2	1	7	70 %

Parmi les cas où l'on a noté une amélioration grâce au Sintrom, l'un d'eux subit une récurrence assez notable au bout de 4 mois, un autre (plutôt inconstant à suivre la thérapeutique) subit quelques récurrences insignifiantes. Les autres se sont trouvés délivrés de toute hémorragie nouvelle.

Quand pourra-t-on commencer le traitement anticoagulant en face d'une hémorragie récente? Nous pensons qu'il est toujours plus prudent d'attendre quelques jours après avoir constaté ophtalmoscopiquement l'arrêt de l'hémorragie.

L'écart entre les séances de photocoagulation et l'établissement de l'hypocoagulabilité ne doit pas être si sévère. En fait l'application correcte de la photocoagulation selon notre avis n'entraîne le danger d'hémorragie que dans le cas d'une augmentation pathologique de la perméabilité capillaire. De toutes façons, il nous paraît préférable de maintenir le taux de coagulation du patient dans les limites de la normalité durant les jours où l'on pratique la photocoagulation ainsi que pendant les deux ou trois jours précédents. Une fois la photocoagulation terminée on revient aux doses qui nous permettent d'atteindre le degré d'hypocoagulation convenable.

Le traitement anticoagulant n'est pas contraire aux médicaments comme la quercétine et la vitamine C qui renforcent la paroi des vaisseaux; nous associons souvent les deux traitements. De même nous ajoutons aussi des injections sous-conjonctivales d'acétate d'hydrocortisone pour lutter contre le facteur hyperergique qui existe d'ordinaire dans la pathogénie de la périphlébite.

Nous employons toutes les deux ou trois semaines 1 cc (25 milligrammes) d'acétate d'hydrocortisone qui avec instillation anesthésique préalable est très bien tolérée.

celui que nous pouvons modifier le plus facilement grâce à notre thérapeutique la polyglobulie en augmentant la viscosité du sang et provoquant leur ralentissement circulatoire favorise la coagulation intravasculaire

Outre la numération globulaire, l'hémogramme et les épreuves courantes de la coagulation et de la perméabilité capillaire, nous cherchons toujours chez nos patients, le temps de prothrombine et le temps d'héparine

Le temps de prothrombine (normal 100%) décode les facteurs extrinsèques, tandis que le temps d'héparine (test de Soulier et de Le Bolloch) décode les facteurs intrinsèques de la coagulation. Rappelons qu'un indice supérieur à 1, pour le temps d'héparine, indique une hypercoagulabilité. Un temps entre 0, 4 et 0, 5 pourrait déjà être dangereux.

Généralement, avec le traitement, les deux valeurs (temps de prothrombine et temps d'héparine) descendent simultanément, mais pas toujours, surtout au commencement du traitement.

Pour obtenir une hypocoagulabilité convenable nous chercherons à prolonger les deux facteurs mentionnés à 1/3 ou 1/2 de leur valeur normale. Un abaissement du temps de prothrombine à 1/2 ou un indice d'héparine à 0, 5 ou 0, 6 seront déjà suffisants.

Pour obtenir l'hypocoagulation, les médicaments les plus recommandables sont, dans notre cas, les cumariques.

Maintenant, le produit cumarinique que nous employons le plus est le "Sintrom", tablettes de 1 mgrs de 3 (4' nitrofuril acetyl cul) + oxycumarine, dont les avantages sont les suivants:

- (1) rapide diminution de l'hypercoagulabilité
- (2) une seule dose par jour "per os" suffit pour maintenir abaissée la coagulation pendant 24 heures,
- (3) en cas de surdosage, la coagulation se régularise rapidement si tôt qu'on arrête le médicament. Celui-ci possède une accumulation minima.

La posologie est la suivante: les premières 24 heures 1 à 6 comprimés, pendant les 24 heures suivantes, 3 comprimés et à partir du troisième jour on doit régler la dose selon le temps de prothrombine. Pour atteindre un temps de prothrombine de l'ordre de 40 à 30%, c'est-à-dire le plus convenable, on doit donner un ou deux comprimés par jour. Après quelques temps, 3/4 de comprimé suffisent. Le contrôle du traitement anticoagulant sera fait quotidiennement les trois premiers jours, tous les deux jours pendant la semaine suivante, ensuite deux fois par semaine et dans la suite du traitement, toutes les deux ou quatre semaines.

Parmi les 59 cas de périphlébite récurrente que nous avons traités depuis 1957, 36 ne l'ont pas été par anticoagulants. Quant aux autres 10, ont été traités avec le Sintrom. Le reste par héparine synthétique sans contrôle méticuleux de la coagulation.



- CARAPANCEA, M, POPESCU, M, PINTILIE I STOIAN M and MIHAI St (Roumania) Retinal agio dynamic aspects in conditions of hypobarism in high altitude pilots
- CARAPANCEA, M, POPESCU M PINTILIE I, STOIAN, M, TEODORESCU, V and STEFAN M (Roumania) Modifications of the visual accommodation in conditions of hypobarism in high altitude pilots
- CARAPANCEA M POPESCU, M RATIU, E, PINTILIE, I STOIAN M and STEFAN M (Roumania) Bulbar conjunctival and corneal sensibility in conditions of hypobarism in high altitude pilots
- CARAPANCEA, M, CARAPANCEA SIMIONESCU, SILVIA and POPESCU, M (Roumania) Ocular manifestations of the mechanism of the action of strychnine on the organism set in conditions of hypobarism at high altitudes
- CARAPANCEA, M, POPESCU M and STEFAN M (Roumania) Les trouble visuels et leurs conséquences sur l'organisme dans les conditions de perception au dispositif radar
- CARAPANCEA, M, CARAPANCEA SIMIONESCU, SILVIA and POPESCU M (Roumania) The mechanism of the modifications of pupillar diameter influenced by myotics on the organism subjected to high altitude hypobarism

### CLINICAL ELECTRORETINOGRAPHY

- BEST, W and REUTER, R (Germany) Frequency analysis of the electroretinogram
- BOUGHIAL, MILAN and KOZOUZEK VLADIMIR (Czechoslovakia) Changements électrorétinographiques à l'état hypnotique
- DEMIRTCIOGLIAN, G G (U S S R) The molecular basis of the origin of the ERG of animals and man
- DEMIRTCIOGLIAN G G, ALLAHVERDIAN M A, BLAVATSKAYA E D and MIRZA AVANIAN I I (U S S R) On the registration of electrical processes in the isolated retina and the optic nerve in cold blooded animals mammals and man
- DIHANDA R P (India) Electro retinography in systemic vascular hypertension
- JACOBSON, JERRY H SUZUKI, TAKASHI and STEPHENS GEORGE (U S A) Use of an averaging computer in analysis of the human ERG
- SUGITA YUICHIRO (Japan) The effects of Serotonin Revertine and JB 516 on the ERG
- VANYSEK JAN and KOZOUSKA VLADIMIR (Czechoslovakia) L Influence de la pupille artificielle sur la grandeur et la forme de l'électrorétinogramme

### DISCUSSION

- ARDEN G B (England) Electro diagnostic test based on the standing potential of the eye
- HATAKEYAMA AKIHI (Japan) Experimental studies on the eye movement by means of simultaneous recording photo electronystagmogram
- HENKES H T and VERDURF P C (Holland) The role of electroretinography and electro oculography in the early diagnosis of tapeto retinal degeneration in children
- TSUTSUYA KOBUKO and ENRI DOMON (Japan) Periodical vibrations on the electromyogram of the extraocular muscles

### INTERNATIONAL ORGANIZATION AGAINST TRACHOMA

- BIETTI G B Presidential address
- BIETTI G B TRFYCHE M J and VOZZA R (Italy) The present distribution of trachoma in the World

The therapy was divided into four groups (Table I)

TABLE I

GROUP A	SUBCONJUNCTIVAL HYDROCORTISONE
GROUP B	SUBCONJUNCTIVAL HYDROCORTISONE + ANDROGENS
GROUP C	SUBCONJUNCTIVAL HYDROCORTISONE + METHIONINE AND CHOLINE
GROUP D	SUBCONJUNCTIVAL HYDROCORTISONE + ANDROGENS + METHIONINE CHOLINE

The cases were divided into 4 groups for purposes of evaluation of effectiveness of the therapy particularly in early cases (Table II)

#### CLASSIFICATION OF CASES

TABLE II

GROUP I	SUDDEN DIMINUTION OF VISION FUNDUS EXAMINATION REVEALS VENOUS DILATATION DISCONTINUITY OF VEINS AND PERIVASCULITIS PRE RETINAL OR RETINAL HAEMORRHAGES
GROUP II	MORE THAN ONE ATTACK OF VITREOUS HAEMORRHAGE MULTIPLE RETINAL AND PRE RETINAL HAEMORRHAGES THIN BANDS OF RETINITIS PROLIFERANS EARLY CHANGES OF PERIVASCULITIS IN THE OTHER EYE
GROUP III	ABOVE CHANGES MORE MARKED
GROUP IV	MARKED RETINITIS PROLIFERANS WITH OR WITHOUT DETACHMENT OF RETINA

Best results were obtained in cases who were given combined therapy (group D) and next in cases treated by group C during the follow up of 6 months to 2 years

The results were assessed on the basis of recurrence rate, period after which recurrence occurred and the residual retinitis proliferans. Cases which did show recurrence the period between the attacks was markedly increased after the start of therapy. Another significant point noted was that one patient who had attack in one eye and showed slight venous dilatation tortuosity or dipping of veins and discontinuity in the other fundus developed haemorrhage in the second eye during the period he was under treatment.

Dans les phases aigües de la périphlébite et après les photo-coagulations, nous nous recommandons dans quelques cas la butadione (Butazolidine) qui, en outre, développe une certaine action anticoagulante.

Il faut se préoccuper de lutter, en même temps, contre les facteurs étiologiques qu'on pourrait déceler dans un cas donné : endocrinopathie, allergie à la toxine tuberculeuse, infection focale, etc.

On ne doit pas oublier que le traitement anticoagulant n'est pas un traitement étiologique, mais un traitement prophylactique.

À ce propos, on peut rappeler que le traitement antituberculeux habituel (streptomycine, hydrazide, etc.) ne modifie pas sensiblement les facteurs de coagulation.

En conséquence, nous estimons que le traitement anticoagulant, appliqué de la façon que nous venons d'expliquer, et la photocoagulation, restent aujourd'hui les deux éléments les plus importants pour combattre la périphlébite rétinienne.

## THERAPY OF EALES'S DISEASE

DR MADAN MOHAN

(Delhi, India)

Therapy and more so prophylaxis of a disease are more important than any of its other aspects. These largely depend upon the knowledge of etiopathogenesis of the condition. The etiology and pathogenesis of Eales's disease has so far been speculative and the treatment empirical and shall remain so till the etiology becomes known.

Various forms of treatment advocated and practised, some of them quite contradictory to one another, range from Yogic exercises to absolute bed rest, anti-tubercular and tuberculin treatment, hormones male and female, coagulants and anticoagulants, roentgen therapy, diathermy and last but not the least photocoagulation.

The choice of treatment largely depends upon the facilities available and the interests of the treating surgeon rather than the actual merit of the treatment for they are all as yet under trial.

On the presumptive etiological theory of hypersensitivity to tuberculo proteins Elliot (1954) suggested the use of subconjunctival hydrocortisone. Encouraged by his results and good reports with androgens and choline we did a comparative study of therapy of sixty (60) cases of Eales's disease.

The bleedings of the vitreous body continued and the centers of phlebitis and peri phlebitis were growing steadily worse

The patient became blind on her right eye owing to an inoperable choroidal cataract due to lack of light perception

Her right eye was on the way of following suit having reached the proliferating stage with thick border lines and an organized peri venous and pre papillary plastic reaction

With blindness imminent, and encouraged by the successful intrafemoral treatment of severe disorders in leg and pelvic veins we requested Dr. Beheran to consider the application of a similar intra carotid treatment

The patient agreed to the treatment, duly notified in advance of the danger involved and of the lack of previous experience

Before starting the treatment, the necessary preliminary tests were made to determine whether the patient was able to tolerate the medication involved

#### Beheran's Technique

After locating the carotid artery on the patient's neck an 18 gauge needle of an average length of 6 centimeters is plunged into the lumen of the artery. The syringe is filled with 10 cc of 1% or 2% novocaine to be injected extremely slowly

The novocaine should be injected very slowly and intermittently to avoid subjective troubles such as feelings of drunkenness, cloudy vision, hallucinations, loss of consciousness. When the shot is over, any symptoms of intolerance should be administered. Should they however be very intense a small intravenous pentothal shot should be administered

If it is done correctly, the patient only feels the peripheral distention of the vessels

After the novocaine injection the needle is kept in the artery and the syringe exchanged for another 10 cc one filled with a solution of the desired antibiotic in 5 or 10 cc of physiological serum or distilled water. After this shot the vascular section should be compressed for a few minutes whereupon the procedure is finished

The treatment has to be administered on an empty stomach with the patient lying on his back

The shot may be repeated at daily or even hourly intervals

From January through March 1953 Dr. Beheran made 7 shots into the right carotid: first 3 penicillin shots and later on upon my request because of the doubtful etiological relationship with TB, he switched to streptomycin administering another four shots. After a 20 day interval another seven shots were administered

This patient has never again had another haemorrhage since 1953. The treatment ended in June 1953. Last examination 10th November 1960, vision on right eye = 20/200 with correction, eye calm, vitreous body clear, plastic periphlebitic and pre papillary sequelae non-evolving. Has remained cured for more than 8 years and subjected to annual check ups

Knowing that the disease tends to be bilateral (56% in present series) we looked for early changes in the veins in the normal eye and all suspected potential cases (8 in the present series) were given subconjunctival hydrocortisone at 6-8 weeks interval. None of these developed any haemorrhage during the period of observation of 6 months to 2 years. A prophylactic use of this therapy in the unaffected eye is therefore, recommended.

## INTRACAROTIDAL TREATMENT OF EALES'S DISEASE A CONTRIBUTION TO ITS STUDY

DR G VON GROLMAN

*Buenos Aires — Argentina*

In studying those intra ocular haemorrhagic diseases that are not caused by arteriosclerosis or by hypertension, we have endeavoured for years to determine the importance of the vein factor and of the humoral factor.

This problem has particularly interested us in the case of diabetic retinosis and of Eales's sickness.

Surprised and encouraged by the excellent results obtained with intra femoral therapy in cases of leg and pelvic vein disorders, we have decided to use similar techniques in exceptional cases of diabetic retinosis and Eales's sickness via intracarotid treatment.

We have tried it out on a few cases of diseased retina due to diabetes — to which I am not going to refer now — and on one case of severe and progressive Eales's sickness which we have followed up for 20 years with exhaustive ophthalmologic studies, both clinical and humoral.

The patient was a 59 year old lady who at that time had been treated by us for 10 years for phlebitis and peri phlebitis of the retina, with repeated haemorrhages of the vitreous body.

In 1943, clinical tests and examinations revealed change of life, focal glomerulonephritis, a slight liver insufficiency, dysproteinemia, blood pressure normal, anaemia, rhinopharynx normal, Brussels test negative, no phobic sequelae, and a slight pre thrombotic condition.

I want to point out that the clinical, humoral, focal radiological and other studies have been conducted in an extremely meticulous manner by colleagues who are top experts in their respective fields.

The patient withstood ten years of severe treatment under the strict supervision of the ophthalmologist, the clinician and the hematologist. The latter (Pavlovsky) treated the slight pre thrombotic condition by means of anticoagulants which proved unsuccessful, as did the anti phobics, the liver protectors, the corticoids, and so on.

A survey of 32 cases of Eales's diseases was made at the Eye Infirmary, Medical College Calcutta at present Institute of ophthalmology, during the past 4 years regarding etiology, complications and treatment

### MATERIALS

All the cases were obtained from the Eye Infirmary, 32 cases showed involvement of 46 eyes. The diagnosis was confirmed on the point of the presence of periphlebitis retinae and retino vitreous haemorrhage. A full history was obtained of both general and local conditions. Routine etiological investigations were carried out for the presence of tuberculosis (screening X ray Chest ESR & Mantoux test 1 in 100 000) blood tests for syphilis, septic foci (teeth ENT), blood count, BT CT urine stool and blood sugar.

Conservative treatments were prescribed for each of them and the effects were followed up. The treatment included a combination of the following

- (i) Anti tubercular therapy with P A S, Streptomycin and Isoniazid
- (ii) Coagulant therapy, with Rutin & Vit C or Calcium gluconate with Vit C or Vit K or styptovit
- (iii) Steroid therapy with prednisolone tablets or A C T H 1 m 10 units twice daily or Retrobulbar injection of decadron

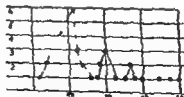
Special treatments included — diathermy coagulation of bleeding area of retina and diathermy for detachment

I have prepared a chart with full details of 32 cases but unfortunately that is too lengthy to be shown here. However, the salient features may be summarised as follows —

### ANALYSIS OF CASES

- I Incidence 32 cases out of 2,760 (1 in 805) eye cases seen. Reported incidence  
1 in 366 (Nederlands Gasthuis voor Ooglydersat Utrecht)  
1 in 1000 to 1500 (Dufour and Gonin)  
6 in 29 000 (Paton)

- II Frequency with age



maximum incidence  
at 22 years of age

- III Sex 3 of 32  
were female



One in every 10

We believe that this is the first case of haemorrhagic vein disorder to be treated and cured intracrotidally, since our bibliographic search for previous records has remained negative.

Of course, it opens up a possibility that may become very valuable and likely to be improved by combining according to the requirements of the case on hand, anti infectious with anti coagulant and anti reactive medication.

We also believe that intracrotidal treatment may become a heroic measure to be taken in thrombophlebitis of the sinus cavernosus.

In the May 1961 issue of the Journal of Angiology, Sussmann and Fitch suggest intracrotidal treatment for administering fibrinolytic enzyme in treating vascular occlusions in the brain.

Vein pathology plays an outstanding part in R D and in diabetic blindness. There is a very numerous R D group in which treatment with anti coagulants is formally indicated. Their association with fibrinolytic enzymes is worthwhile studying.

In very severe cases of retinosis, with relapses of large scale haemorrhages, advanced impairment of vision, persistent damage due to phlebitis and a relative soundness of the arterial system, the indication of intracrotidal treatment should be resorted to as an exceptional and heroic measure after the other methods of treatment have failed.

This indication is subject to the extent to which the arterial system has been affected, and to the encephalic and other afore mentioned conditions. Intracrotidal treatment is indicated in Lyles's sickness whenever its severity warrants it. In cases of thrombophlebitis of the sinus cavernosus, its early application is worthwhile considering.

The therapeutic requirements of the vein condition within the eye may be discarded by clinical counter indications, but they ought not to be disregarded because of lack of extra ocular semiological corroboration.

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## LYLES'S DISEASE      GENERAL OBSERVATION

DR N N CHANDA

*Institute of Ophthalmology,*

*Calcutta, India*

Lyles's disease is a fairly common malady in Bengal. The interest of the ophthalmologists has been drawn to solve the problem of its etiology and treatment throughout the world but as yet no definite conclusion has been arrived at (P C Donders 1958). Various sorts of treatment were suggested by various workers. These included coagulation (diathermy as well as light) of the diseased vessels. Apart from symptomatic treatment and treatment of complications other treatments would mean an empirical one.

A survey of 32 cases of Fuchs's diseases was made at the Eye Infirmary Medical College Calcutta, at present Institute of ophthalmology, during the past 4 years regarding etiology, complications and treatment

### MATERIALS

All the cases were obtained from the Eye Infirmary, 32 cases showed involvement of 46 eyes. The diagnosis was confirmed on the point of the presence of periphlebitis retinal and retino vitreous haemorrhage. A full history was obtained of both general and local conditions. Routine etiological investigations were carried out for the presence of tuberculosis (screening X ray Chest ESR & Mantoux test 1 in 100 000) blood tests for syphilis septic foci (teeth EN 1), blood count, B T C T urine stool and blood sugar.

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maximum incidence at 22 years of age

III Sex 3 of 32 were female

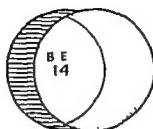


One in every 10



## IV Ocular preponderance

R E 8



left eyes were Only involved in 10 cases

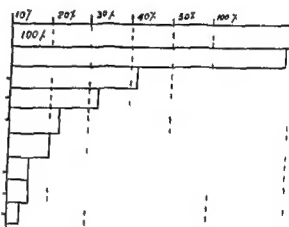
right eyes were Only involved in 8 cases

Both eyes were involved in 14 cases

V Trauma Vague history of previous injury to one eye were obtained in two cases of binocular incidence

## VI Feature and Complications

- (a) Periphlebitis retinae 100% cases and always peripheral
- (b) Retinal haemorrhage 99%
- (c) Vitreous haemorrhage 32%
- (d) Retinitis proliferans 23%
- (e) Retinal detachment 13%
- (f) Patches of old chorioretinitis 10%
- (g) New vessels at disc 6%
- (h) Cataract complicated 6%
- (i) Old iritis 4%



## VII Result of investigations

- 1 Mantoux skin test 1 in 100 000
- 2 X ray of thorax
- 3 ESR (Westergren)
- 4 Nasal allergy
- 5 Septic tooth septal ulcer
- 6 Blood tests for syphilis (K B & W R)

POSITIVE	NEGATIVE
14 CASES 70%	6 CASES 30%
PIRRO C LES ON 3 30	7-70%
H GH 2 2	23 78%
3 10	29 90%
3 10	29 90%
3 10	30 93%

## RETINAL DETACHMENTS

As its incidence was found fairly high (13%) six cases of retinal detachments were further scrutinised. In all cases detachment were localised in the lower half of the globe irrespective of the situation of the vascular lesion. No definite tear could be detected in any one of them. In two of them bands of retinitis proliferans were noted and in one an old patch of choroiditis was associated. Detachment appeared late in the course of the disease.

### TREATED DETACHMENTS

Three cases were operated upon and surface diathermy was applied with penetrating diathermy to drain out fluid. Case No. 1 showed postoperative small haemorrhage at 12 O'clock position followed by profuse vitreous haemorrhage after a few weeks. Case No. 2 also developed postoperative vitreous haemorrhage. Case No. 3 developed postoperative profuse vitreous opacities and ended in endophthalmitis.

### UNTREATED DETACHMENTS

Three detachments were only treated conservatively. Case No. 1 detachment became total. Case No. 2 retina flattened after a month. Case No. 3 remained unchanged.

### SURFACE DIATHERMY OF BLEEDING VESSELS

Diathermy coagulation of bleeding areas of retina is a known method of treatment to stop further bleeding (Weve 1935, 1939, Franceschetti A and Forni S (1954a)). Four cases were selected for this purpose. A surface diathermy just to produce visible whitening of the fundus was applied over the area of affection about one fourth circumference of the eye between the equator and ora serrata under conjunctival flap. Good results were obtained. In all cases bleeding was arrested, blood showed absorption and in none recurrence of haemorrhage has occurred yet.

### CASES NOT TREATED BY SURFACE DIATHERMY

The remaining 39 cases which had no surface diathermy but were treated by conservative method showed the following results:

- (a) blood showed quick absorption — 17 eyes — 43 per cent
- (b) no change in 12 eyes — 30 per cent
- (c) fresh haemorrhage in subsequent attack — 10 eyes — 25 per cent

### COAGULATION BY LIGHT

A light coagulation is of great help in preventing haemorrhage in vitreous as any area of periphlebitis can be coagulated long before the haemorrhage takes place.

### CONCLUSION

Incidence of Eales's disease is fairly high in Bengal. Apart from high incidence of positive mantoux test no other positive etiological finding had any significant incidence.

Among the treatments heat coagulation of diseased vessels proved to be of some value. Diathermy treatment in retinal detachments however proved unsatisfactory.

## SUMMARY

46 eyes of Eales' disease were analysed regarding incidence, age frequency, sex, ocular preponderance and results of conservative therapy and special therapy including surface diathermy to stop bleeding vessels and surface diathermy to treat detachment of retina.

Diathermy treatment for retinal detachment was not found favourable but that for bleeding vessels showed satisfactory results.

## ACKNOWLEDGEMENT

I am grateful to Prof. Dr. K. L. Sen, Director, Institute of Ophthalmology, Medical College, Calcutta for guidance and help.

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